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COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS IN PEDIATRIC AGE GROUP

(A HOSPITAL BASED OBSERVATIONAL STUDY)

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ABBREVIATIONS

1. BAL-Bronchioalveolar lavage.
2. LTBI- Latent TB infection.
3. CBNAAT-Cartridge Based Nucleic Acid Amplification Test.
4. GA-Gastric Aspirate.
5. AFB-Acid fast bacilli .
6. RNTCP- Revised National Tuberculosis Control Programme.
7. NTEP-National Tuberculosis Elimination Program.
8. IGRA- Interferon Gamma Release Assay.
9. ATT-Anti Tuberculosis Therapy.
10. WHO- WORLD HEALTH ORGANISATION.
11. DBT-Direct Benefit Transfer.
12. LAM- Lipoarabinomannan.
13. PPD- Purified protein derivative.
14. NAAT- Nucleic acid amplification techniques.
15. TST-Tuberculin skin test.
16. ADA- Adenosine deaminase.
17. ZN-ZiehlNeelsen.
18. HRCT- High-resolution computed tomography.
19. POCT-Point-of-care testing.
20. MTB-Mycobacterium tuberculosis.
21. TMA-Transcription-Mediated Amplification.
22. LPA-Line probe assay

23. PCR- Polymerase Chain Reaction.

24. SDA- Strand displacement amplification.

25. RT-PCR- Reverse transcription-polymerase chain reaction.

26. NASBA- Nucleic Acid Sequence-Based Amplification.

27. FIND- Foundation for Innovative New Diagnostics.

28. MDR TB- Multidrug-Resistant Tuberculosis.

29. XDR TB- Extensively Drug-Resistant Tuberculosis.

30. FLQ- Fluoroquinolones.

31. LFX- Levofloxacin.

32. MFX- Moxifloxacin.

33. ES- Endotracheal Suction.

34. IS- Induced Sputum.

35. NPA- Nasopharyngeal Aspirate.

36. AUC- Area Under the Curve.

37. PPE- Personal Protective Equipment .

38. DST-Drug sensitivity testing .

39. MGIT- Mycobacterium Growth Indicator Tube.

INTRODUCTION

INTRODUCTION

Tuberculosis remains a significant global health challenge, in terms of both mortality and morbidity. In 2020, approximately 10 million people were affected by TB worldwide, including 1.1 million children. Around two-thirds of all TB cases were concentrated in just eight countries, with India bearing the largest burden[1].By 2023, an estimated 10.8 million new TB cases were recorded globally. In India, the rate of microbiologically confirmed pulmonary tuberculosis in individuals aged 15 and older was 316 cases per 100,000 people in 2022[2].

Untreated mortality rate of tuberculosis is approximately 50%, butcure can be achieved by comprehensive anti-tubercular therapy in about 85% of individuals who do not have rifampicin resistance[3].

Diagnosis can be made in a suspected case of TB by direct visualization of AFB in smear or culture or NAAT (Nucleic acid amplification techniques).It can be indirectly made in a patient with suggestive history and signs based on tuberculin skin test,radiology, and blood counts, ESR or ADA[4].

Improving the efficiency and accuracy of TB diagnosis contributes to treatment efficacy in a suspected case. In 1882, Sir Robert Koch discovered tubercle bacilli and was later awarded the Nobel Prize in 1905 for his work[4].Despite over a century passing since this breakthrough; tuberculosis (TB) remains a challenging disease to diagnose. Initially, clinical diagnosis was the focus, but it quickly became apparent that the symptoms and signs of TB are nonspecific[4].

With the advent of X-ray imaging by Wilhelm Rontgenin 1895 chest X-rays became a valuable diagnostic tool. However, radiological findings alone are not always definitive for TB [5,6].

In children perihilar or paratracheal lymphadenopathy is the radiologic hallmark of primary infection in childhood. However homogeneous consolidation like any pneumonia, obstructive atelectasis or over inflation from compression by an adjacent enlarged node canoccur. Bronchiectasis and formation of cavities or miliary tuberculosis may also be seen[7.] Sometimes a normal x ray may show findings on HRCT[7, 8].

Sputum smear microscopy using Ziehl-Neelsen (ZN) staining remains a widely used laboratory method for TB detection. This technique has been in use for over a century[9,10,11].It **is** inexpensive and specific but lacks sensitivity. Also, efficacy is operator dependent, resulting in a broad range of sensitivities and specificities reported in various studies, 25.3–81.6% and 83.4–99% as compared to gold standard[12]. Further it is even less sensitive in high-risk groups .e.g., HIV, and children. However positive predictive value and negative predictive value was 94.1% and 93.9% respectively[12].

Culturing TB in solid media **(e.g.,** Lowenstein–Jensen or Middlebrook 7H11) remains the gold standard. However, it requires long time of25.1–25.5 days[13]. Culturing in liquid media (**e.g.,** for use with the BACTEC Mycobacterium Growth Indicator Tube (MGIT) 960 system) shortens the duration. However, it still takes about two weeks[14]**.**Sub-optimal laboratory facilities in resource-limited settings often restrict practical use of culture methods.

An ideal diagnostic test for TB would be rapid, affordable, standardized, easily performed at the point of care, automated (requiring minimal training) test which is safe with minimal bio-safety risks, and possess satisfactory sensitivity, specificity, and predictive values[15]. POCT refers to medical diagnostic testing conducted outside of a laboratory, near the patient.

In 2010, the World Health Organization (WHO) endorsed two molecular diagnostic tests for TB and drug-resistant TB: the MTBDR-plus line probe assay (LPA) and Xpert MTB/RIF (CBNAAT). . India's Revised National Tuberculosis Control Programme (RNTCP) has adopted CBNAAT for use at district and sub-district levels and LPA at national and regional levels**[16]**.The GeneXpert MTB/RIF (CBNAAT) is an automated real-time PCR assay designed for the rapid and simultaneous detection of MTB and 'RIF' resistance within 2 hours. CBNAAT can also detect rifampicin (RIF) resistance. The test utilizes single-use plastic cartridges with multiple chambers that are preloaded with liquid buffers and lyophilized reagent beads [11]. Detection threshold of smear is 10,000 org/mL, Liquid culture is 50–100 org/mLand CBNAAT is100–150 org/mL[17].

In a pediatric study of cases of pulmonary and extrapulmonary tuberculosis CB-NAAT detected 100% of smear positive cases. The sensitivity, specificity, PPV and NPV of CB-NAAT in clinically diagnosed pulmonary cases was 60%, 100%, 100% and 65.8% respectively

with diagnostic accuracy of 80.2%. In subjects with clinically diagnosed tuberculosis, Mycobacterium tuberculosis culture was positive in 18.9 % cases, AFB smears in 12.1% whereas CB-NAAT was positive in 55.4% cases[18].

TB diagnosis in children continues to be a challenge due to many reasons like difficulty in getting appropriate samples, Paucibacillary disease and relatively high incidence of extrapulmonary TB[17].

For pulmonary TB, sputum is the most important sample for laboratory testing and it may be collected as sputum-induced or expectorated. However young children may not be able to produce or give sputum sample. Here gastric aspirate (GA) has been used as sputum is swallowed by young children[17].The other alternative samples available are: laryngeal swabs, bronchioalveolarlavage (BAL), nasopharyngeal aspirate, etc.

According to reports, gastric aspirate (GA) samples had the highest (40-92%) detection rate. Detection rates for other samples were from 4-43% for BAL, 24-30% for nasopharyngeal aspiration, 27-63% for a laryngeal swab, and 20-30% when utilizing induced sputum. Thus, GA and induced sputum are important samples for the diagnosis of pediatric pulmonary TB[19].

One study done in pediatric patients showed that in pulmonary samples, CBNAAT detected tubercular bacilli in 21.4% sputum/induced sputum samples and in 33% gastric lavage/aspirate samples[**20**].

In another study, based on the clinical, radiological, and microbiological profile, 23/50 suspected children were diagnosed with pulmonary TB. If Gastric aspirate was used alone, the yield was 11 cases (47.8%). If sputum (expectorated or induced) was used alone, the yield was 12 cases (52.1%). The difference in the two yields was not statistically significant (p = 1). The combined yield of GA and sputa was 69.5%, which was significantly more than when either of the specimens was used alone[21].

In another study for children, GA showed superior diagnostic capacity to expectorated sputum, induced sputum, or Nasopharyngeal aspirate[22].

An interesting study by Douglas L et al showed that there was no correlation between the age and yield of CBNAAT from GA. BAL did not increase the yield any further. However, in adult studies which used lower dose of lidocaine showed BAL to be superior to GA for diagnosis of TB by CBNAAT[23]. This study was done in 1992. Since then, there have been hardly any studies to show whether there are additional benefits of BAL CBNAAT in patients who are negative for GA for CBNAAT or comparative efficacy of GA and BAL CBNAAT. Therefore, this study was planned to see if in suspected cases of pulmonary tuberculosis in children based on history examination and other indirect tests like Mantoux, X ray/CT, blood investigations etc whose GA is negative for CBNAAT, does BALCBNAAT diagnose additional cases.

AIM AND OBJECTIVES

AIM AND OBJECTIVES

AIM:

"To compare the positivity of detection of Mycobacterium Tuberculosis with CBNAAT in BAL fluid and Gastric aspirate to diagnose Pulmonary Tuberculosis in pediatric age group".

OBJECTIVES:

- To Detect Mycobacterium in BAL fluid
- To Detect Mycobacterium in Gastric Aspirate
- To compare the yield from BAL fluid and Gastric Aspirate

CBNAAT

NEED FOR THE STUDY:

- CBNAAT of BAL fluid may detect M Tuberculosis in a suspected case of Tuberculosis, when the sputum smear is negative for AFB and CBNAAT for Gastric aspirate are negative
- It is very difficult in Pediatric tuberculosis to detect Mycobacterium as tuberculosis as it is Pauci bacillary in Pediatric age group and sample collection particularly sputum collection is very difficult. The NTEP guidelines mention that every effort should be made to detect Mycobacteriae by various investigation methods before starting ATT if Clinical condition is permissible
- CBNAAT gives faster result compared to sputum culture and it is more sensitive than microscopic smear examination, hence ATT can be initiated as soon as possible.
- Detecting Rifampicin resistance will help to treat drug resistance and to start appropriate ATT

REVIEW OF LITERATURE

REVIEW OF LITRATURE

Epidemiology: Global Burden of Tuberculosis

Tuberculosis (TB) remains a significant global health challenge, comparable to HIV/AIDS in terms of both mortality and morbidity. In 2020, approximately 10 million people were affected by TB worldwide, including 5.5 million men, 3.3 million women, and 1.1 million children. Around two-thirds of all TB cases were concentrated in just eight countries, with India bearing the largest burden. Despite a global decline in TB incidence by 11% from 2015 to 2020, TB still caused 1.5 million deaths in 2020, a reduction from 2.4 million deaths in 2000. The latest analysis of epidemiological survey in India has provided an estimate of 226 per 1000 (22.6%) for the burden of TB infection for population aged above 15 years[1].The recent systematic review and meta-analysis concluded 24.8% global prevalence of LTBI based on IGRA**[1].** The Interferon Gamma Release Assay (IGRA) based Latent TB infection (LTBI) prevalence for the South East Asia region was reported as 36% (95%CI: 25.3 – 46.7)**[1]**.Reports from our country showed about one-fourth of the population has TB infection was a matter of concern and needs to be addressed in the context of TB elimination**[1]**.Males were more likely to have TB infection **[23,24,25]** .This possibly could be attributed to sociological factors**[25]**. A meta-analysis which included 2.2 million from 56 TB prevalence surveys over 28 countries concluded that TB prevalence is higher among men than women**[26]**. Similar observation has been reported from an earlier study in household contacts which documented LTBI prevalence of 77% in individuals aged 15–18 years and 85% in persons aged > 45 years. Increased frequency of social contacts and use of public transits leading to increased exposure could be contributing to higher LTBI prevalence with advancing age. These findings suggested that older age groups need to be sensitized about TB. TB case detection be actively undertaken and be considered for intervention with TB preventive therapy**[27]**.States especially those with high TB infection rates (> 30%) which include Delhi, Telangana, Uttar Pradesh, Punjab, Chandigarh, Karnataka have to identify the possible reasons and plan appropriate targeted interventions**[28].**Individuals residing in urban location were more likely to have TB infection**[29].**Annual risk of TB infection of 2.2% in the urban compared to 1.3% in the rural areas has been reported in an earlier study from India[29]. This could be attributed to overcrowding, slums, migrant population in urban settings**[30]**. This enforces that individuals with past history of TB have to be closely evaluated by active case finding periodically and considered for TB preventive strategies. Body mass index was not associated with TB infection in the recent epidemiological studies**[31]**.Under-nutrition leads to poor immune response and tests for LTBI are likely to be negative. Under-

nutrition fuelling the TB burden is well documented and WHO estimated that globally, 1.9 million TB cases are attributed to undernutrition[32]. Cognizant of the burden of under-nutrition and TB, the TB programme of India has introduced Direct Benefit Transfer (DBT) for nutritional support to TB patients (Ni-kshay Poshan Yojana)[32].

Tuberculosis Burden in India

In India, the rate of microbiologically confirmed pulmonary tuberculosis in individuals aged 15 and older was 316 cases per 100,000 people in 2022[2]. The incidence varied significantly, with Delhi recording a peak of 534 cases per 100,000 and Kerala seeing a low of 115 cases per 100,000. In 2020, 16,281,161 TB cases were reported, a number that rose to 19,333,381 in 2021[24]. The National TB Prevalence Survey Report published in 2020 also revealed an 11% increase in the TB death rate between 2019 and 2020[33].

Structure of Mycobacteria

Mycobacteria appear as slender, curved rods in stained clinical specimens. Their cell wall is made up of mycolic acids, complex waxes, and unique glycolipids. The typical structure of the M. tuberculosis cell wall, along with other mycobacteria, is depicted in Fig1.The cell wall of Mycobacterium tuberculosis plays a crucial role in the bacterium's virulence. Mycolic acids are considered key contributors to the bacterium's virulence and have extremely long side chains (C60 to C90), which are linked to the muramic acid component of the peptidoglycan via phosphodiester bridges and to arabinogalactan through esterified glycolipid linkages. Variations in species are often due to differences in the sugar substitutions within the glycolipids or peptidoglycolipids. The cord factor, produced most abundantly in virulent strains of M. tuberculosis, forms chains of cells that resemble serpentine cords when grown in vitro. These structures are crucial to the bacterium's ability to evade the immune system.

The mycobacterial cell wall is acid-fast, meaning it retains carbolfuchsin dye even after being decolorized with acid-ethanol. This key feature allows for differential staining in clinical samples, such as sputum. Other important components of the cell wall include trehalosedimycolate (also known as the cord factor, which induces serpentine cord formation in artificial media) and mycobacterial sulfolipids, which may play a role in virulence. Additionally, lipoarabinomannan (LAM) is a unique constituent that may contribute to pathogenesis. Structural differences in purified LAM from virulent and attenuated strains of mycobacteria could influence their ability to stimulate cytokine production in mononuclear cell cultures.

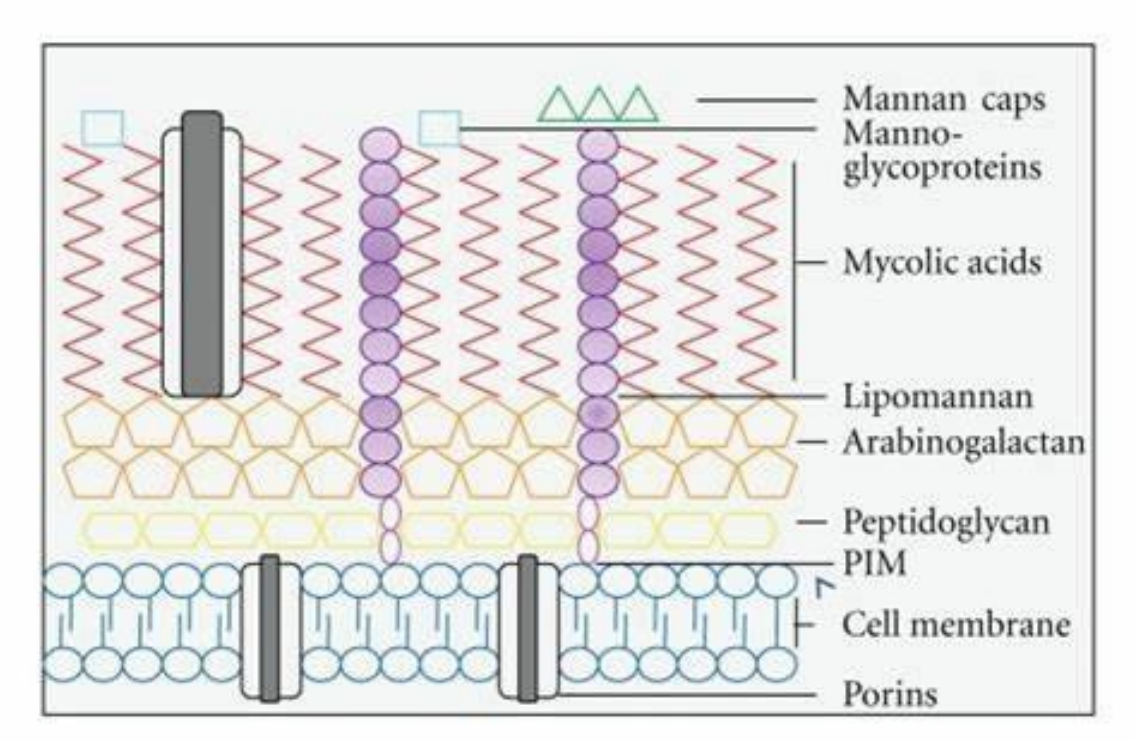

Fig 1: Complex cell wall structure of Mycobacterium TB

Optimum pH and Temperature

Mycobacterium tuberculosis thrives at 37°C, with growth ceasing below 25°C and above 40°C. The optimal pH range for growth is between 6.4 and 7.0. M. tuberculosis is more sensitive to acidic pH than M. magmatism, which has a more efficient internal pH regulation mechanism[34].

Effect of Physical and Chemical Agents

Mycobacterium tuberculosis can survive in sputum for 20-30 hours. The bacteria are killed at 80°C in 15-20 minutes and instantly at 100°C. Direct exposure to sunlight for two hours can

also kill the bacteria. While M. tuberculosis is sensitive to ultraviolet (UV) light, it is relatively resistant to many chemical disinfectants. It can survive exposure to 5% phenol, 15% sulfuric acid, 3% nitric acid, 5% oxalic acid, and 4% sodium hydroxide. However, it is sensitive to formaldehyde and glutaraldehyde, and can be destroyed by tincture of iodine in 5 minutes and by 80% ethanol in 2-10 minutes.

The Genome of Tuberculosis

The genome of M. tuberculosis H37Rv, the laboratory standard strain, has been fully sequenced. It has 4,411,532 base pairs, with 3924open reading frames.

Pathogenesis of tuberculosis

During a TB infection, M. tuberculosis reaches the pulmonary alveoli, where it is phagocytosed by alveolar macrophages. The macrophages recognize the bacteria as foreign and attempt to eliminate them through phagocytosis. Once engulfed, the bacteria are contained in a membrane-bound vesicle known as a phagosome. This phagosome then fuses with a lysosome to form a phagolysosome, where the bacteria can be destroyed. However, M. tuberculosis is able to survive and replicate within the macrophage. TB transmission often occurs through the inhalation of infectious droplets expelled when an infected person coughs. These droplets contain the bacteria, which can spread to others, including through hematogenous dissemination to other tissues in the body[35].

Clinical suspicion of TB

The initial sign of a new Mycobacterium tuberculosis infection is often the conversion of an intradermal skin test using purified protein derivative (PPD) to positive or the incidental discovery of a lesion on a chest x-ray in an otherwise asymptomatic individual. Clinical symptoms develop in only a small percentage (5-10%) of people. Those who do develop symptoms typically present with pulmonary disease, characterized by a chronic, productive cough, low-grade fever, night sweats, fatigue, and weight loss. Tuberculosis can also present with extrapulmonary manifestations, such as lymphadenitis, kidney, bone, or joint involvement, meningitis, or disseminated (miliary) disease. Lymphadenitis and meningitis are

more common in infants with tuberculosis, while all extrapulmonary manifestations occur more frequently in immunocompromised individuals, including patients on chronic renal dialysis, the elderly, malnourished individuals, and those living with HIV[34].

Diagnosis of TB

Direct Evidence

• Microscopy for detection of acid fast bacilli (AFB)
• Culture for isolation of M. Tuberculosis bacilli
• Nucleic acid amplification techniques (NAAT)
• Antigen detection

Indirect Evidence

• Tuberculin skin test (TST): Used as a complementary test along with history symptoms, signs and
radiology.
• Interferon-gamma release assay (IGRA)
• Antibody detection tests: Serological tests for TB are banned by
WHO since July 2011 and are not recommended for diagnosing TB.
• Radio diagnosis: Chest X-ray is used as a screening tool. CT scan
in very selected cases
• Cytology and histopathology
• Others: CBC, ESR, ADA[17].

Diagnosis of tuberculosis should be considered if there is: - [12].

- Fever and or cough for > 2 weeks
- History of weight loss more than 5% or no weight gain in past 3months
- Hilar lymphadenopathy on chest skiagram
- Tuberculin skin test positivity
- Coexistence of precipitating illness
- Abdominal USG suggestive of tuberculosis
- ADA positivity in pleural fluid
- CSF findings consistent with tubercular meningitis
- Cranial CT suggestive of tuberculoma

In an adults study, cough was present in 100% patients, fever in 93%, sputum in 93% and loss of weight and appetite was present in 62% patients[36].In another study on young adults less than 30 years cough was the most common symptom in 81.82% of the patients followed by fever in 56.64%, weight loss in 46.85%, decreased appetite in 41(28.67%), breathlessness in 18.88% and hemoptysis in 17.48% patients. 12(8.39%) of patients had history of contact with the TB patient sand 67(46.85%) of patients had previous history of tuberculosis[37].In a pediatric study Mean Age was 7.93 (±-4.79) years with a range of 4 months–17 years. Pulmonary TB accounted for 85 (56%) and EPTB 66 (44%) cases. Mean age of PTB/EPTB was 6.85 (±4.46) and 9.32 (±4.87) years respectively. Among 66 children with EPTB, neuro TB (TB meningitis + tuberculoma) accounted for 20[38]. According to the WHO the most common signs and symptoms of childhood TB are: chronic cough that has not improved for 21 days with or without wheezing; fever >38°C for 14 days, when other common causes, including pneumonia, have been excluded; objectively documented weight loss or failure to thrive; feelings of sickness or weakness, lethargy, and/or reduced playfulness; and night sweats. There may be pleural effusion, cavitation and collapse or consolidation. Extrapulmonary tuberculosis may present as Lymphadenopathy including hilar lymphadenopathy, Gibbus formation in vertebral tuberculosis, meningitis, pericardial effusion, a distended abdomen with ascites, and signs of tuberculin hypersensitivity (e.g., phlyctenular conjunctivitis or erythema nodosum)[39].

Improving the efficiency and accuracy of TB diagnosis contributes to treatment efficacy in a suspected case. In 1882, Sir Robert Koch announced the discovery of tubercle bacilli to a small group of scientists, and was later awarded the Nobel Prize in 1905 for his work[4]. Despite over a century passing since this breakthrough, tuberculosis (TB) remains a challenging disease to diagnose. Initially, clinical diagnosis was the focus, but it quickly became apparent that the symptoms and signs of TB are nonspecific[4].

With the advent of X-ray imaging by Wilhelm Röntgenin the year 1895 chest X-rays became a valuable diagnostic tool; however, no radiological findings are specific to TB [5, 6.] The hot cathode X-ray tube which used thermionic emission was patented in 1913 and produced in 1917 by GE by William D. Coolige; thus, the design of the modern tube is still called and referred to as the Coolige tube[40].

Consolidation, infiltrates, Cavity or collapse with consolidation, fibrosis, pleural effusion or pneumothorax, miliary pattern, ground glass opacity or normal x- ray -may be seen in adults [36,37, 38]. On HRCT-thorax, these normal CXR were found to have bronchiectatic changes, small

centrilobular nodules, miliary mottling, and ground glassing which were not visible on the Chest X-rays. The other patterns mentioned above refers to emphysematous changes, bulla, air crescent sign, pleural effusion, and bronchiole found in a minority[8].Regarding radiological findings in children peri-hilar or paratracheal lymphadenopathyis the radiologic hallmark of primary infection in childhood. Homogeneous consolidation, obstructive atelectasis or over inflation from compression by an adjacent enlarged node can occur. Fibrosis and destruction of the lung parenchyma result in traction bronchiectasis and formation of cavities. Miliary tuberculosis is seen in 8% of cases, usually in the younger age group because of immature immune function. It is an acute hematogenously disseminated infection presenting as innumerable ≤2-mm non-calcified nodules scattered in both lungs[7].

The standard laboratory diagnostic method for tuberculosis remains the microscopic examination of sputum smears for tuberculous bacilli, a technique that has been in use for over a century[9]. This method provides critical information for confirming a diagnosis and evaluating the patient's contagiousness. Ziehl–Neelsen (ZN) staining microscopy is a fundamental diagnostic tool, particularly in settings where resources and equipment for bacterial culture are limited[10]. This approach is rapid and effective in identifying cases with a high bacterial load, which also indicates a higher risk of transmission.

This staining method was initially introduced by Paul Ehrlich (1854–1915) and subsequently modified by the German bacteriologists Franz Ziehl (1859–1926) and Friedrich **Nee**lsen (1854–1898) during the late 19th century[11]. It **is** inexpensive and somewhat specific but lacks sensitivity. Efficacy is operator dependent, resulting in a broad range of sensitivities and specificities reported in international studies, 25.3–81.6% and 83.4–99% as compared to gold standard [12]. It is even less sensitive in high-risk groups, such as patients with HIV, and children. However positive predictive value and negative predictive value was 94.1% and 93.9% respectively[12].

Methods to improve efficacy include use of mercury vapour fluorescence and light-emitting diode (LED) microscopy, which have largely replaced traditional ZN staining. Similar to culture, direct microscopy remains an integral part of monitoring response to treatment, measuring infectiousness, and predicting likelihood of relapse in patients who are smear positive at diagnosis.

Culturing TB in solid media(e.g. Löwenstein–Jensen or Middlebrook 7H11) remains the gold standard, although it requires considerable time (25.1–25.5 days) [13]. Culturing in liquid media

(e.g. for use with the BACTEC Mycobacterium Growth Indicator Tube (MGIT) 960 system) shortens the duration but still takes about two weeks [14]. However sub-optimal laboratory facilities in resource-limited settings often restrict its practical use. While culture is not recommended for use as a first-line test, it remains an important part of TB diagnostics where persistent culture positivity can predict likelihood of relapse.

High-resolution computed tomography (HRCT) and other radiological techniques can reveal anatomical changes in the lungs and other organs, but they cannot definitively diagnose TB[41].Like all infectious diseases, diagnosing TB relies on isolating the causative organisms or their nuclear products[42].

An ideal diagnostic test for TB would be rapid, affordable, standardized, easily performed at the point of care (POCT), automated (requiring minimal training), safe with minimal bio-safety risks, and possess satisfactory sensitivity, specificity, and predictive values[15]. POCT refers to medical diagnostic testing conducted outside of a laboratory, near the patient.

Molecular diagnostic tests meet many of these criteria. These tests, which detect the nucleic acids of organisms, are fast and provide results within hours. They can identify Mycobacterium tuberculosis (MTB) complex from cultured samples or directly from clinical specimens[43]. Additionally, they can detect drug-resistant strains. Various nucleic acid amplification tests (NAATs) are available, including polymerase chain reaction (PCR), transcription-mediated amplification (TMA), line probe assays (LPA), strand displacement amplification (SDA), nucleic acid sequence-based amplification (NASBA), reverse transcriptase (RT)-PCR, and CBNAAT (cartridge-based NAAT), among others[44].

The World Health Organization (WHO) has endorsed the MTBDR-plus (LPA) and Xpert MTB/RIF (CBNAAT) for rapid TB and drug-resistant TB diagnosis. India's Revised National Tuberculosis Control Programme (RNTCP) has adopted CBNAAT for use at district and sub-district levels and LPA at national and regional levels[16]. Detection threshold of smear is 10,000 org/mL, Liquid culture is 50–100 org/mLand CBNAAT is100–150 org/mL[17].

Polymerase Chain Reaction (PCR), developed by Kary Mullis in 1993, is a key molecular diagnostic technique. In PCR, a biological sample is heated to denature the double-stranded DNA into single strands. After cooling, a specific primer is introduced to form a template-primer complex [45].The sensitivity and specificity of PCR in TB are 95 and 98%, respectively in smear positive for acid-fast bacilli (AFB) respiratory specimens, and they are 75 to 88 % and 95 % respectively in smear negative culture positive for MTB respiratory specimens.PCR is more sensitive than a smear but less sensitive than culture for diagnosis of TB. PCR may be positive in dead and dormant bacilli, so it does not always indicate active TB. Also,

contamination and laboratory errors can cause false positive results. On the contrary, a negative PCR result is not sufficient to exclude TB. It has been observed that PCR positivity may vary from sample to sample. PCR is less accurate if the patient had ATD before. The presence of inhibitors like haemin, globulin, beetle nut, etc. can cause false negative results. PCR has the problem of high cost, and it is not a POCT.

Xpert MTB/RIF Assay (CBNAAT/GeneXpert): The Gene-Xpert has been developed by the Foundation for Innovative New Diagnostics (FIND) in 2009[46]. The Xpert MTB/ RIF assay has been approved by WHO in 2010 and US FDA in 2013 for the diagnosis of tuberculosis in patients getting less than 7 days of therapy[46]. It is a fully automated and quick test (results obtained by 2 hours) that requires minimum bio-safety and training. CBNAAT can also detect rifampicin (RIF) resistance. The GeneXpert MTB/RIF is an automated real-time PCR assay designed for the rapid and simultaneous detection of MTB and 'RIF' resistance within 2 hours. The test utilizes single-use plastic cartridges with multiple chambers that are preloaded with liquid buffers and lyophilized reagent beads. Clinical samples are treated with sodium hydroxide and isopropanol-containing reagent at 3:1 ratio for sputum pellets and at 2:1 ratio for unprocessed sputum samples. Then, they are incubated at room temperature for 15 minutes. The treated sample is then manually transferred to the cartridge, and then that is loaded into the gene Xpert instrument. Subsequent processing is fully automated.

Mycobacterium tuberculosis is detected by the five overlapping molecular probes (probes A–E) that collectively are complementary to the entire 81 bp rpo core region. MTB is identified when at least two of the five probes give positive signals with a cycle threshold (CT) of d"38 cycles. CT is the number of multiplication of DNA that is required for the detection of DNA of MTB[47].The basis for detection of RIF resistance is the difference between the first (early CT) and the last (late CT) M. tuberculosis-specific beacon (ÄCT).

In December 2010, the WHO recommended the widespread use of the Xpert MTB/RIF assay, with a policy statement issued in early 2011 to support rapid implementation. This guidance included technical instructions and operational considerations, along with a checklist of necessary prerequisites for successful implementation.

In a large multicentric study in 2015 including 1730 patients in Peru, Azerbaijan, South Africa, and India with suspected tuberculosis, the test correctly identified 98% smear-positive tuberculosis and 72% smear-negative/ culture-positive tuberculosis[48]. Mono-resistance to RIF is rare and at least 90% of all RIF-resistant clinical isolates are also resistant to INH. Hence, a positive result for RIF resistance is used as a strong surrogate of multi-drug resistant (MDR)-TB. RIF resistance outside rpoβ gene is rare and it has been shown that up to 95 to 98% RIF

resistance is caused by mutations in the rpoβ gene. The CRS included a NAAT (other than Xpert), histology, smear, biochemical testing results, presenting signs and symptoms or response to treatment with anti-TB therapy in addition to culture[49].

Following the WHO's recommendation; there was an unprecedented global uptake of this technology and by December 2013, more than 2,000 GeneXpert instruments and over 5 million Xpert MTB/RIF cartridges had been procured in 98 countries eligible for concessional pricing Xpert sensitivity differed substantially between sample types[50]. In lymph node tissues or aspirates, Xpert pooled sensitivity was 83.1% (95% CI 71.4 to 90.7%) versus culture and 81.2% (95% CI 72.4 to 87.7%) versus CRS. In cerebrospinal fluid, Xpert pooled sensitivity was 80.5% (95% CI 59.0 to 92.2%) against culture and 62.8% (95% CI 47.7 to 75.8%) against CRS. In pleural fluid, pooled sensitivity was 46.4% (95% CI 26.3 to 67.8%) against culture and 21.4% (95% CI 8.8 to 33.9%) against CRS. Xpert pooled specificity was consistently 98.7% against CRS across different sample types. One study done in pediatric patients showed that in pulmonary samples, CBNAAT detected MTB in 21.4% sputum/induced sputum samples and in 33% gastric lavage/aspirate samples[20].

For extra-pulmonary samples, the detection rates were 12.7% for CSF samples, 10% for pleural fluid samples and 66.7% for lymph node aspirate samples[51].They found that in pediatric population sensitivity, specificity, positive predictive value and negative predictive value of CBNAAT in reference to culture were 92.7%, 98.9%, 97.1%, and 97.2% respectively, and those were 100%, 90.68%, 71.42%, and 100% respectively in reference to Ziehl-Neelsen (ZN) smear[52].The introduction of the Xpert MTB/RIF assay has significantly advanced the fight against TB, particularly in resource-limited settings, and has the potential to dramatically improve early detection and treatment outcomes for both TB and MDR-TB.While recommended for use, it is important to remember these assays have reduced sensitivity in certain populations such as children and patients co-infected with HIV, as well as in extrapulmonary TB.

In terms of diagnostic performance, a study by Sharma SK et al. from AIIMS, India, demonstrated that CBNAAT had an overall sensitivity of 95.7% and specificity of 99.3% for pulmonary TB. For smear-negative, culture-positive cases, the sensitivity was 77.7%. The test also showed a high sensitivity of 94.5% and specificity of 97.7% for detecting rifampicin resistance, with even better results when compared to gene sequencing (sensitivity 99.0%, specificity 99.3%). These findings underscore the promising potential of CBNAAT, offering reduced uncertainty in diagnostic results[53].

CBNAAT plays an equally important role in diagnosis of TB in smear negative samples as discussed in study shown by K.N Mohan Rao et al.in which 80 clinically significant patients with AFB smear Negative status gave CBNAAT positive in 29 which was 30% positivity[33]. A study by M.singh et al **[62]**showed the useful ness of Genexpert in Diagnosis of TB in pediatrics from North Indian medical colleges with promising results in which out of 50 children with age group of 0-14 23 were diagnosed TB the rest were clearly negative for TB when tested by culture and with the gold standard the sensitivity and specificity was 84.6% and 86.4% respectively**[54.]** . A study conducted in South Africa by G Theoron et al in 2011 and in 496 patients from a high HIV prevalence setting in which Xpert MTB/RIF detected 95% of smear-positive culture-positive cases and the specificity was 94%. Whenin comparison to smear microscopy Xpert MTB/RIF detected an additional 17 cases giving a rise of 18% in the rapid TB case detection[5]. Performance of CBNAAT in FNAC was discussed by Biadglegne F from Ethiopia in which 231 FNAC were tested in which the Xpert test in relation to culture identified 29 from 32 culture positive, 5 from 11 with contaminated results, and 56 from 188 culture negative results. The overall sensitivity of the test was 93.5% and specificity 69.2%[6.] .All the studies clearly show that CBNAAT changed the story of TB diagnosis from day's months to hours and with high sensitivity and specificity and to add finding the unknown which would likely get missed.

In addition, it is essential that there is emphasis on early detection of potential drug resistance. Drug resistance is a growing issue that threatens TB care worldwide. Traditionally this was categorized into rifampicin-resistant TB (RR-TB), multidrug-resistant TB (MDR-TB) or extensively drug-resistant TB (XDR-TB). MDR-TB is resistant to both rifampicin (RIF) and isoniazid (INH). Recently definitions have been updated to include pre-XDR-TB, which is TB that fulfils the definition for MDR-TB and RR-TB that is also resistant to any fluoroquinolone (FLQ).

The updated definition for XDR-TB is strains that fulfil the definition for MDR-TB/RR-TB which are also resistant to any group A drug (namely levofloxacin (LFX), moxifloxacin (MFX), bedaquiline (BDQ) and linezolid (LZD), Replacing the old XDR-TB definition referencing second-line injectable drugs (SLID), it highlights the trend towards use of oral regimens comprising recently developed or repurposed drugs. Despite the importance of early recognition, only 61% of patients with a new diagnosis of bacteriologically confirmed TB disease in 2019 were tested for RIF resistance. This is in part related to access to diagnostics

in resource-limited settings. There are numerous methods currently available, and under development, to determine drug resistance. For these diagnostics to be beneficial on a global scale they need to provide timely, accurate, cost-effective results in centres where access to power, equipment and technical expertise remains limited [54].

In a meta-analysis comparing 15 studies which included 4768 respiratory specimens from 3640 children, pooled sensitivities and specificities of Xpert for tuberculosis detection were 62% (95% credible interval 51–73) and 98% (97–99), respectively, with use of expectorated or induced sputum samples. Pooled sensitivities and specificities of Xpert for tuberculosis detection were found to be 66% (51–81) and 98% (96–99), respectively, with use of samples from gastric lavage. In these studies, Xpert was compared to culture[55].

In a pioneering Indian study, from different centres,4,600 paediatric presumptive pulmonary TB cases were enrolled, which diagnosed 590 (12.8%, CI 11.8–13.8) pediatric PTB cases. Overall, 10.4% (CI 9.5–11.2) of presumptive PTB cases were detected by Xpert MTB/RIF, in comparison to 4.8% (CI 4.2–5.4) smear-positive results. Also, upfront Xpert MTB/RIF testing of presumptive PTB and presumptive DR- TB cases detected 79 and 12 rifampicin resistance cases, respectively clearly showing its utility for programme.

Usefulness of Xpert for detecting TB among infants was demonstrated in a multi-centric Indian study. 7994 presumptive infant TB cases were enrolled, among which 462 (5.7%) were TB positive on Xpert, of which of which only 89 (19.3%) were positive on smear microscopy, only 3 cases were detected on microscopy but negative on Xpert. Overall, 26 (5.6%) of infants diagnosed with TB, were found to be rifampicin-resistant.

Detection of AFB in sputum samples under optimal conditions is somewhere between 10^4 and 10^5 bacilli per ml. ZN staining has a low sensitivity of 22–43% for single smear, but increases with 2 smears. Even though AFB stain of sputum is positive in up to 75% of adults with pulmonary TB, fewer than 20% of children with TB have a positive AFB smear of sputum or gastric aspirate[55].

In a pediatric study of cases of pulmonary and extrapulmonary tuberculosis CB-NAAT detected 100% of smear positive cases. The sensitivity, specificity, PPV and NPV of CB-NAAT in clinically diagnosed pulmonary cases was 60%, 100%, 100% and 65.8% respectively with diagnostic accuracy of 80.2%. In subjects with clinically diagnosed tuberculosis, Mycobacterium tuberculosis culture was positive in 18.9 % cases, AFB smears in 12.1% whereas CB-NAAT was positive in 55.4% cases[18].Line probe assay is for detection of Mtb resistance is line probe assay (LPA). Genotype MTBDRplus and Genotype MTBDRsl

are used for the detection of Mtb and its associated drug resistance. The WHO approved Genotype MTBDRplus employs a series of steps to detect Mtb and mutations in rpoB and katG, which confer RIF and INH resistance, respectively. Additionally, it can detect the presence of inhA promoter genes that confer resistance to low dose INH, which are also typically associated with ETH and prothionamide resistance. This in vitro test delivers results in <6 h. When compared with traditional culture-based drug sensitivity, it is 78.5% sensitive and 100% specific at detecting RIF and INH resistance. The WHO endorsed Genotype MTBDRsl 2.0 assay can also detect resistance conferring mutations of FLQ (gyrA and gyrB) and SLID (rrs and eis). Reported sensitivity and specificity are 100% and 98.9% for FLQ, and 89.2% and 98.5% for SLID. Even more sensitive than NAAT at detecting FLQ resistance, this rapid test could allow for use of FLQ in patients that might otherwise have faced a lengthier regime that potentially required the interim use of SLID. However, these tests are not without limitations including low sensitivity for detecting ethambutol (ETM) and aminoglycoside resistance as demonstrated in a real-world analysis. Similar in aim to the Xpert MTB/XDR assay, these LPAs provide prompt recognition of drug resistance, so patients can be started on the appropriate regimen and further drug resistance does not have an opportunity to develop while awaiting standard culture-based susceptibility results, nor are patients exposed to burdensome, longer drug regimens with higher potential for toxicity **[56]**.

Culture-based drug sensitivity testing (DST) -Major advantage of liquid culture is rapidity of growth, which has led to more widespread use of liquid broth-based methods such as the MGIT. BACTEC MGIT 960 is a fully automated system that delivers results within 2 weeks. Culture-based DST remains the gold standard for determining drug resistance at present. The two approaches currently in use are the critical concentration and minimum inhibitory concentration (MIC). Classically, critical concentration was defined as the lowest concentration of a drug that inhibits growth of 95% of mtb strain present.

Owing to ongoing research, these critical concentrations are regularly: updated with a recent reduction in the critical concentration required to determine RIF resistance, allowing for greater concordance between genotypic and phenotypic sensitivity results.

Alternatively, the MIC method is defined as the lowest concentration of a drug that results in complete inhibition of visual growth of the Mtb strain in vitro. Following extensive work completed by national reference laboratories, and international discussion and agreement, a new reference MIC protocol has been set and validated by European consortia[57].

TB diagnosis in children continues to be a challenge due to many reasons, namely:

• Difficulty in getting appropriate samples,

• Paucibacillary disease,

• Relatively high incidence of extrapulmonary TB [17.]

Sample collection methods

For pulmonary TB, sputum is the most important sample for laboratory testing and it may be collected as sputum-induced or expectorated, or gastric aspirate (GA) [17.] The other alternative samples available are: laryngeal swabs, bronchioalveolar lavage (BAL), nasopharyngeal aspirate, etc. According to reports, gastric aspirate (GA) samples had the highest (40-92%) detection rate. Detection rates for other samples were from 4-43% for BAL, 24-30% for nasopharyngeal aspiration, 27-63% for a laryngeal swab, and 20-30%when utilizing IS. Thus, GA and IS are important samples for the diagnosis of pediatric pulmonary TB[19].

The sensitivity, specificity, PPV, NPV, and accuracy of CBNAAT against MGIT were 75.0%, 94.4%, 80.0%, 92.7%, and 90.0% respectively for GA samples. The sensitivity, specificity, PPV, NPV, and accuracy of CBNAAT against MGIT were 63.64%, 96.6%, 77.8%, 93.44%, and 91.42% respectively for IS samples[19]. Other studies reported similar results.

Out of the 70 samples of GA, 15 (21.4%) were positive by Xpert assay, six (8.57%) were positive for AFB in smear microscopy, and 16 (22.9%) were obtained to be culture positive. Out of 16 culture-positive GA samples, CBNAAT was able to detect 12 cases. Out of 10 culture-positive cases, which were negative in the smear, CBNAAT diagnosed only seven cases and the remaining three were negative by CBNAAT. Moreover, three samples were smeared- and culture-negative was detected positive by GeneXpert[19].

A study by Douglas L et al showed there was no correlation between the age and yield of CBNAAT from GA. BAL did not increase the yield any further. In adult studies which used lower dose of lidocaine showed BAL to be superior to GA(600 mg versus 200-320 mg). But in this pediatric study lidocaine 60 mg in 2 cases only. Amount of saline instilled, technical difficulty in children for doing BAL may affect results[23].

In a review of 50articles, the respective sensitivity and specificity ofXpert MTB/RIF were [22].

	Sensitivity	Specificity
Adult BAL	87% (95% CI: 0.84–0.89),	95% (95% CI: 0.93–0.97)
Adult ES group	90% (95% CI: 0.88–0.91),	97% (95% CI: 0.95–0.99)
Adult IS group	86% (95% CI: 0.84–0.89)	97% (95% CI: 0.96–0.98
pediatric ES group	14% (95% CI: 0.10–0.19	99% (95% CI: 0.97–1.00)
Pediatric IS group	67% (95% CI: 0.62–0.72)	99%(95% CI: 0.98–0.99)
Pediatric GA group	80% (95% CI: 0.72–0.87)	94% (95% CI: 0.92–0.95)
Pediatric NPA group	54% (95% CI: 0.43–0.64)	99% (95%CI: 0.97–0.99)

For children, GA sample showed superior diagnostic capacity compared to ES, IS, or NPA samples. In this systematic review, ES provided better diagnostic performance (sensitivity, specificity, andAUC) than BAL or IS for adult PTB. Since both BAL and IS had a higher bacterial load than ES, they should theoretically provide better diagnostic performance than ES. It may be due to smaller volume of IS, ranging from 0.5 to 2 ml, whereas the volume of ES ranges from 1 ml to more than 2 ml. sampling from one or two parts of lung led to poor repeatability and limited detection rate when taking BAL. For paediatric PTB, similar specificity and AUC appeared when using IS and GA as sample, nonetheless, Xpert MTB/RIF showed much higher sensitivity when using GA as sample to diagnose pediatric PTB[22].

In a study of 100 children <12years (majority < 5 years) culture positive tuberculosis was found in 21% children. The sensitivity, specificity, positive predictive value and negative predictive value for CBNAAT were 76.1%, 98.7%, 94.1% and 93.9% and for ZN stain were 47.6%, 98.7%, 90.9% and 87.6% respectively. Positive history of contact (p value 0.0217), reactive Mantoux test (p value < 0.001) and low socioeconomic status were independently associated with a positive CBNAAT result[58]. Positive history of contact was found in 33% while 67% had no history of contact.

Procedures like gastric aspiration, NPA, and sputum induction are classified as aerosol-generating. While children with TB disease are generally less infectious than adults, transmission can still occur, especially in those with extensive pulmonary involvement[59].

When performing these procedures on children who may be infectious (e.g., those with persistent coughing, extensive lung damage, or cavitary TB), the following bio safety measures must be followed:

- **Room Setup**: Perform the procedure in a dedicated cough room with proper directional airflow (6-12 air exchanges per hour).
- **Personal Protective Equipment (PPE)**: All personnel must wear particulate respirators (N95 or FFP2), eye protection, gloves, and disposable plastic aprons. Caregivers assisting during the procedure should also wear PPE.
- **Signage**: Display a sign outside the room to prevent unauthorized entry during the procedure.
- **Hand Hygiene**: Wash hands according to local protocols before and after the procedure. Disinfect all surfaces with 70% alcohol solution before and after the procedure.
- **Sample Handling**: Ensure specimen containers are tightly closed, disinfected on the outside before labelling, and placed in sample bags for transport.
- **Post-Procedure Clean-Up**: Dispose of masks, gloves, and aprons in appropriate bins and disinfect hands immediately after discarding PPE. Wait 10 minutes before leaving the room, and close the door immediately after exiting.

Expectoration

1. Explain the purpose and process of sputum collection to the child and family.
2. Instruct the child to rinse their mouth to remove any food or bacteria.
3. Ask the child to take deep breaths, holding each breath briefly before exhaling slowly. On the third breath, they should cough deeply and produce sputum.
4. If sputum production is insufficient, encourage the child to cough again until enough sample is obtained.
5. If sputum cannot be produced, dispose of the container appropriately.

Gastric Aspiration

In young children, TB bacteria may be swallowed in mucus and remain in the stomach, making gastric aspiration a useful method for sample collection. This procedure is especially helpful for diagnosing TB in children who cannot produce sputum.

Materials Needed

- Non-sterile gloves, particulate respirators (N95), eye protection, disposable aprons, nasogastric tubes (6-10 French), syringes, sterile specimen containers, sodium bicarbonate solution, litmus paper, etc.

Contraindications

- Child not fasted for 4 hours
- Low platelet count or other bleeding issues
- Obstructive lesions in the nasopharyngeal tract

Procedure

1. Ensure the child has fasted for at least 4 hours before the procedure.
2. Prepare all materials and disinfect surfaces.
3. Position the child comfortably and use an assistant to help stabilize the child during the procedure.
4. Instill a local anesthetic gel in the nasogastric tube to minimize discomfort.
5. Insert the nasogastric tube, aspirate gastric contents using a syringe, and check the pH of the aspirate with litmus paper.
6. If no fluid is obtained, perform a gastric lavage using sterile water or saline.

Neutralize the sample with equal volume of sodium bicarbonate to neutralize the acidic gastric contents to prevent the destruction of tubercle bacilli and transport it to the laboratory for testing in a cool box to the laboratory for processing as soon as possible (within 4 hours). Otherwise, it should be placed in the refrigerator (4–8°C) and stored until transported[17].

Bronchoscopy and bronchoalveolar lavage (BAL) can be used as a technique for specimen collection in much selected cases. It should not be used up front and as a standalone test as the yield is no better than GA. It is available at higher centres only and should be restricted in children with persistent pneumonia/non responding pneumonia as a part of work up. In sputum smear-negative and Pauci bacillary patients with clinico-radiological features of PTB Xpert® MTB/RIF has good sensitivity for diagnosis on BAL fluid. It is useful even when cultures are negative[17].

In a study, out of 43 patients, in 16.2% induced sputum was CBNAAT positive even though adequate sputum was produced. In same patients BAL showed 62.8% positive for CBNAAT[36]. In another study of patients under 30 years, out of 93 cases of PTB, 87(93.5%) patients were Xpert MTB/RIF assay positive, 80(86.0%) were AFB culture positive and 39(41.9%) patients

were AFB smear positive. The sensitivity and specificity of BAL Xpert MTB/RIF assay was 92.5% and 79.37% respectively (p <0.0001)[37].

In yet another adult study the sensitivity and specificity of AFB smear in BAL fluid was found to be 48.86% and 85.14% respectively. The PPV value was 79.63% and NPV was 58.33%. The sensitivity and specificity of CBNAAT/MTB gene X-pert assay was 78.89% and 95.83% respectively; with a PPV of 95.95% and NPV of 78.41%. Out of the 74 CBNAAT positive cases, the number of rifampicin sensitive cases were 65 (65/74, 87.84%) and rifampicin resistant cases were 9 (9/74, 12.16%). Authors commented that performing CBNAAT/gene X-pert in BAL fluid in sputum smear negative pulmonary tuberculosis improves PTB case detection as well as Rifampicin resistance and augments diagnosis, clearly outperforming AFB smear[8.]

After consent, fifty children aged 0–14 years with suspected PTB were enrolled. Sputum/induced sputum and gastric lavage from the participants were collected on two consecutive days. Bronchoalveolar lavage was also done if indicated. The microbiological isolation in these specimens by Smear, MGIT culture, or X-pert MTB/RIF assay was compared. Based on the clinical, radiological, and microbiological profile, 23/50 children were diagnosed with PTB. If GLA was used alone, the yield was 11 cases (47.8%).

If sputum (expectorated or induced) was used alone, the yield was 12 cases (52.1%). The difference in the two yields was not statistically significant (p = 1). The combined yield of GA and sputa was 69.5%, which was significantly more than when either of the specimens was used alone. Sputum was induced in 11 children, who could not expectorate. GLA and IS were compared, as these are the typical specimens obtainable in children who cannot expectorate. The yield of GLA was 4/11(36.36%) in these samples, and it was 5/11 (45.45%) for IS. Combining GLA and IS increased the yield to 7/11(63.6%) which amounted to a 27.2% increase from using GLA alone. Induced sputum is a valuable tool to increase the microbiological yield for the diagnosis of PTB in young children who cannot expectorate and should be considered routinely [21].

BAL is the process of instilling and recovering a volume of saline into the distal airways through bronchoscope to ensure that the returned fluid contains material originally present on the alveolar surface. BAL serves as a type of liquid biopsy for the distal airways, providing objective evidence of infectious or inflammatory processes.

There are two types of BAL: non-bronchoscopic and bronchoscopic. Non-bronchoscopic BAL involves inserting catheters or balloon-type devices through an endotracheal tube. In contrast, bronchoscopic BAL uses a flexible bronchoscope to instill and immediately withdraw sterile saline (0.9% NaCl), typically targeting the middle lobe or lingula. BAL fluid (BALF) analysis measures various components, including the percentage of saline recovered and cellular or non-cellular content.

Equipment Preparation:

Before starting the BAL procedure, the bronchoscopy cart must be brought to the bedside, and all equipment must be checked for functionality. Essential equipment includes:

- Bronchoscope and light source
- Swivel adapter, biopsy, and suction valves
- Bite block
- Gauze and water-soluble lubricant
- Wall suction and tubing
- Saline for irrigation and suction port cleaning
- Non-bacteriostatic saline (for lavage)
- 20 ml Luer-Slip syringes
- Five total aliquots of saline
- Sterile bowl and sputum trap
- Sterile drapes and towels for patient coverage
- Protective gear: gloves, gown, mask, face shield

Pre-Procedure:

Prior to the procedure, a thorough pre-anesthetic evaluation is necessary, which includes assessing the child's medical history, conducting a physical examination, and reviewing lab results. The anesthetist should explain the anesthesia plan to the parents and ensure that the child has fasted as required. Infants under one year should fast for at least 6 hours if fed formula, 4 hours if breastfed, and 2 hours after consuming only clear fluids.

Children over one year old should fast for 6 hours after eating solid foods or milk, and 2 hours after consuming clear fluids.

Anesthetic techniques must be tailored to the child’s condition, considering factors such as physical status, airway assessment, and any underlying conditions like respiratory infections. General anesthesia risks must be minimized, so the American Society of Anesthesiologists’

physical status classification should be applied. Medication must ensure adequate sedation for comfort and procedure tolerance, using a combination of opioids, benzodiazepines, or propofol. Additionally, patients requiring bronchoscope insertion through an endotracheal tube must be administered paralytics to avoid scope damage.

Procedure:

There are two main techniques for performing BAL: non-bronchoscopic and bronchoscopic. Non-bronchoscopic BAL involves using catheters or balloon devices through an endotracheal tube. Bronchoscopic BAL, on the other hand, involves using a flexible bronchoscope to instill and withdraw normal saline. The preferred areas for BAL in diffuse lung diseases are the middle lobe and lingula due to their smaller size, which facilitates better fluid recovery. In cases of localized lung disease, BAL targets the affected lobe or segment, and in cystic fibrosis, multiple site samples may be required.

To prevent contamination, BAL should be performed before any other bronchoscopic procedures. A gentle suction technique is applied while maintaining the bronchoscope wedged in the target site, with pre-warmed saline (37°C) instilled and withdrawn. The amount of saline used varies according to the patient's weight, with some methods suggesting 2–4 aliquots of 10–20 ml per aliquot for children, while others recommend up to 10% of the child's functional residual capacity.

Monitoring: Continuous monitoring by Pulse oximetry, ECG, and Blood pressure was done.

Post-Procedure: the bronchoscope should be cleaned by suctioning an enzymatic detergent solution through the suction port. The scope is then wiped with a detergent-soaked sponge and placed in a biohazard bag. A post-procedure chest x-ray is typically required to assess for complications.

Processing of BAL Fluid: BAL fluid must be kept at 4°C to preserve its cell viability. The first aliquot is often sent for microbiological studies, while subsequent aliquots are filtered and pooled for cytological analysis. Depending on the clinical needs, the fluid may be processed for bacterial, viral, or fungal cultures. Cytospin preparations or resuspension and centrifugation of the BALF can be used to assess cell counts and morphology. Specialized stains may be employed for specific conditions, such as Oil Red O for lipid-laden macrophages or iron staining for alveolar hemorrhage.

BAL fluid composition can be influenced by several factors, including the lavage site, fluid pH, and volume of saline used. Proper precautions, such as anaerobic transport for bacterial cultures, are essential to avoid contamination and ensure accurate results.

Analysis of gastric aspirate samples with CBNAAT is sensitive and specific methods for rapid diagnosis of pulmonary tuberculosis in children who cannot produce sputum but instead swallow their sputum. Aspiration or lavage of gastric content is best procedure in them for obtaining specimen from which to culture Mycobacterium tuberculosis[12]. As compared to IS where 16.2% CBNAAT positive, BAL showed 62.8% CBNAAT positivity **[60]**.L.Saglam et al, found that bronchial washings smear was positive in 53% of cases.**[12,60]**.

MATERIALS AND METHODS

MATERIAL & METHODS:

Study design: Hospital based Observational Study

Place of study: Pediatric department
Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh

Study population: Clinically suspected cases of pulmonary tuberculosis both Inpatient and Outpatient will be enrolled in the study after their consent.

Duration of the Study: 1 year.
Size: Sample size was 45
The subjects were divided into two groups based on the sample material for CBNAAT test as BAL group and Gastric Lavage group in the study. Sample was collected from BAL fluid and Gastric aspirate group for patients.

The samples were sent for CBNAAT
The data was analysed and the results were then compared between the two groups.

INCLUSION CRITERIA

Children with respiratory symptoms and X- ray chest suggesting tuberculosis in the form of Cavity, mediastinal lymph nodes, collapse, consolidation, opacities not responding to antibiotics, pleural and or pericardial effusion.

Children aged below 18 years with symptoms of persistent cough and/ or persistent fever for more than two weeks and/ or unexplained weight loss for more than 5% in the last three months

Children in contact with adult pulmonary tuberculosis before starting TPT (Treatment to prevent tuberculosis), to rule out active tuberculosis

In case of persistent respiratory symptoms & chest X ray is showing opacity but not specific to TB like collapse, consolidation, cavity and mediastinal lymphadenopathy wee included.

In case of infants born to mother having pulmonary tuberculosis during pregnancy and/ or diagnosed pulmonary tuberculosis after delivery were included to rule out active disease before TPT.

Children under 18 years of age with significant superficial lymphadenopathy not explained by other causes were included.

EXCLUSION CRITERIA

Patients above the age of 18 years of age with symptoms of tuberculosis

Patients aged above 18 years, who were known to have tuberculosis and were on anti-tubercular treatment were included.

Patients aged above 18 years of age who are having relapse, default and failure of treatment were included.

The sample size for "COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS IN PEDIATRIC AGE GROUP" was 37, was calculated according to the formula given by Wan NorAriffin.

Sample Size Calculation for Sensitivity and Specificity Estimation

- Expected Sensitivity: 0.8
- Expected Specificity: 0.8
- Disease Prevalence (p): 0.42
- Precision (± Expected): 0.2
- Confidence Level (1-α): 95%
- Expected Dropout Rate**:** 10%

Based on these parameters:

- Sample size for sensitivity (nSen): 37
- Sample size for specificity (nSpec): 37
- Final required sample size (largest value): 37
- Final sample size (with 10 % dropout),n drop=42

https://wnarifin.github.io/ssc/sssnsp.html

Formula reference:

Buderer, N. M. F. (1996). Statistical methodology: I. Incorporating the prevalence of disease into the sample size calculation for sensitivity and specificity. Academic Emergency Medicine, 3(9), 895-900.

Suggested reference:

APA: Arifin, W. N. (2025). Sample size calculator (web). Retrieved from http://wnarifin.github.io

Vancouver: Arifin WN. Sample size calculator (web) [Internet]. 2025 [cited 1 April 2025]. Available from: http://wnarifin.github.io

CLINICAL STUDY PROTOCOL

The assessment of each patient was conducted following a comprehensive approach, which included the following steps:

1. Detailed History and Clinical Examination: A comprehensive history and clinical examination were conducted, including demographic information such as age, sex, socio-economic status, and whether the patient resided in a rural or urban area. Additionally, any prior history of tuberculosis or exposure to a tuberculosis patient was documented. .

2. Routine Blood Investigations: Standard blood tests were adviced for all patients.

   All the parameters:

   Hemoglobin (Hb),

   Total Leucocytes Count (TLC),

   Platelets count

   ESR

3. Other Investigations Required:

   HIV,

   HbsAg,

   HCV

   LFT

   RFT

   Smear and CBNAAT

4. Radiological Assessment: Radiological examination of the lesion was performed, which included a chest X-ray (PA view) for all patients. Patients having neck swelling were also subjected to X-ray imaging. In certain cases, where necessary and feasible, CT scans or MRIs were done.

5. Sputum Analysis: If sputum was available, Ziehl-Neelsen (ZN) staining was performed to check for Mycobacterium tuberculosis.

6. Gastric aspirate for CBNAAT

7. CBNAAT (Cartridge-Based Nucleic Acid Amplification Test): The aspirate was also tested using the CBNAAT method, utilizing the Xpert MTB/RIF system manufactured by Cepheid, which is endorsed by the WHO (2010). The test was done with the manufacturer's instructions. The sample treated with a reagent containing NaOH and also isopropanol in a 2:1 ratio and allowed to sit at room degree temperature for 15 minutes, then occasional movements. Three milliliters of this made sample was transferred into a falcon tube container, which then placed in the CBNAAT machine. The automated machine completed the remaining assay steps, and the results were displayed on the connected monitor after approximately 1 hour and 50 minutes.

8. Rifampicin Resistance Detection: Samples which detected for Mycobacterium tuberculosis were further analyzed for Rifampicin resistance using, Line Probe Assay (LPA). The LPA procedure involved three process: The process involved DNA extraction, multiplex PCR amplification, followed by reverse hybridization..

This multi-step diagnostic process was aimed at accurately identifying tuberculosis and assessing its resistance to Rifampicin, enabling appropriate treatment and management.

COLLECTION OF SAMPLES

GASTRIC ASPIRATION

Background:

In young children, TB bacteria may be swallowed in mucus and remain in the stomach, making gastric aspiration a useful method for sample collection. This procedure is especially helpful for diagnosing TB in children who cannot produce sputum.

Materials Used:

- Non-sterile gloves, particulate respirators (N95), eye protection, disposable aprons, nasogastric tubes (6-10 French), syringes, sterile specimen containers, sodium bicarbonate solution, litmus paper, etc.

Contraindications:

- Child not fasted for 4 hours
- Thrombocytepenia or other bleeding issues
- Obstructive lesions over the nasopharyngeal tract

Procedure:

7. Ensure the child has fasted for at least 4 hours before the procedure.
8. Prepare all materials and disinfect surfaces.
9. Position the child comfortably and use an assistant to help stabilize the child during the procedure.
10. In still a local anesthetic gel in the nasogastric tube to minimize discomfort.
11. Insert the nasogastric tube, aspirate gastric contents using a syringe, and check the pH of the aspirate with litmus paper.
12. If no fluid is obtained, perform a gastric lavage using sterile water or saline.
13. Neutralize the sample with sodium bicarbonate and transport it to the laboratory for testing.

BRONCHOALVEOLAR LAVAGE (BAL):

Bronchoalveolar lavage (BAL) is a critical diagnostic tool used in bronchoscopy, defined as the process of instilling and recovering a volume of saline into the distal airways to ensure that the returned fluid contains material originally present on the alveolar surface. This fluid includes both soluble and cellular elements from the alveolar and small airway surfaces. BAL serves as a type of liquid biopsy for the distal airways, providing objective evidence of infectious or inflammatory processes. The procedure was first popularized in 1974 by American physicians Reynolds and Newball in Maryland.

Bronchoalveolar lavage (BAL) facilitates the retrieval of both cellular and non-cellular elements from the epithelial lining fluid (ELF) within the alveolar and bronchial airspaces. It can be performed using two methods: non-bronchoscopic and bronchoscopic BAL. Non-bronchoscopic BAL involves inserting catheters or balloon-based devices through an endotracheal tube, whereas bronchoscopic BAL utilizes a flexible bronchoscope to instill and aspirate sterile saline (0.9% NaCl), typically targeting the middle lobe or lingula. The analysis of BAL fluid (BALF) includes assessing the percentage of saline recovered along with its cellular and non-cellular content.

BAL serves diagnostic, therapeutic, and research purposes, with its most common application in diagnosing infectious diseases in children. Other indications include evaluating non-specific chronic respiratory symptoms, unexplained radiological findings, or suspected interstitial lung disease. BAL is regarded as the gold standard for detecting and diagnosing chronic pulmonary aspiration. While generally safe and well-tolerated, some patients may experience transient side effects like fever, cough, or pulmonary infiltrates, which typically resolve within 24 hours.

Equipment Preparation:

Before starting the BAL procedure, the bronchoscopy cart must be brought to the bedside, and all equipment must be checked for functionality. Essential equipment includes:

- Bronchoscope with an integrated light source
- Swivel adapter, biopsy tool, and suction valves
- Protective bite block

- Sterile gauze and water-based lubricant
- Wall-mounted suction unit with tubing
- Saline solution for irrigation and cleaning the suction port
- Non-bacteriostatic saline (for lavage)
- 20 ml Luer-Slip syringes
- Five total aliquots of saline
- Sterile bowl and sputum trap
- Sterile drapes and towels for patient coverage
- Protective gear: gloves, gown, mask, face shield

Pre-Procedure:

Before the procedure, a comprehensive pre-anesthetic evaluation is essential. This includes reviewing the child's medical history, conducting a physical examination, and assessing laboratory findings. The anesthetist must also explain the anesthesia plan to the parents and ensure adherence to fasting guidelines. Infants under one year should fast for at least 6 hours after formula feeding, 4 hours after breastfeeding, and 2 hours after consuming clear fluids. For children older than one year, fasting should be maintained for 6 hours after solid food or milk intake and 2 hours after clear fluids. Anesthetic techniques must be tailored to the child's condition, considering factors such as physical status, airway assessment, and any underlying conditions like respiratory infections. General anesthesia risks must be minimized, so the American Society of Anesthesiologists' physical status classification should be applied. Medication must ensure adequate sedation for comfort and procedure tolerance, using a combination of opioids, benzodiazepines, or propofol. Additionally, patients requiring bronchoscope insertion through an endotracheal tube must be administered paralytics to avoid scope damage.

Procedure:

There are two main methods for performing BAL: non-bronchoscopic and bronchoscopic. Non-bronchoscopic BAL involves using catheters or balloon devices through an endotracheal tube. Bronchoscopic BAL, on the other hand, involves using a flexible bronchoscope to instill and withdraw normal saline. The preferred areas for BAL in diffuse lung diseases are the middle lobe and lingula due to their smaller size that facilitates better fluid recovery. In cases

of localized lung disease, BAL targets the affected lobe or segment, and in cystic fibrosis, multiple site samples may be required.

To prevent contamination, BAL should be performed before any other bronchoscopic procedures. A gentle suction technique is applied while maintaining the bronchoscope wedged in the target site, with pre-warmed saline (37°C) instilled and withdrawn. The amount of saline used varies according to the patient's weight, with some methods suggesting 2–4 aliquots of 10–20 ml per aliquot for children, while others recommend up to 10% of the child's functional residual capacity.

Monitoring:

Continuous monitoring is crucial throughout the procedure to ensure hemodynamic stability and adequate oxygenation. Standard monitoring includes:

- Pulse oximetry
- Continuous ECG
- Blood pressure monitoring every 5 minutes or continuously
- Documentation of sedation and paralysis details, signed by the attending physician

Post-Procedure:

After the procedure, the bronchoscope should be cleaned by suctioning an enzymatic detergent solution through the suction port. The scope is then wiped with a detergent-soaked sponge and placed in a biohazard bag. A post-procedure chest x-ray is typically required to assess for complications.

Processing of BAL Fluid:

BAL fluid must be kept at 4°C to preserve cell viability. The first aliquot is often sent for microbiological studies, while subsequent aliquots are filtered and pooled for cytological analysis. Depending on the clinical needs, the fluid may be processed for bacterial, viral, or fungal cultures. Cytospin preparations or resuspension and centrifugation of the BALF can be used to assess cell counts and morphology. Specialized stains may be employed for specific conditions, such as Oil Red O for lipid-laden macrophages or iron staining for alveolar haemorrhage.

The composition of BAL fluid can vary depending on factors such as the lavage site, fluid pH, and the volume of saline instilled. To maintain sample integrity and ensure accurate results,

Precautions like anaerobic transport for bacterial cultures are crucial in preventing contamination

Fig 2: BAL PROCDEDURE BEING PERFORMED AT O.T

CBNAAT RESULTS

On completion of a test run, the Cartridge-based Nucleic Acid Amplification Test (CBNAAT) gives the following results:

1. **MTB DETECTED; Rif Resistance DETECTED**
2. **MTB DETECTED; Rif Resistance NOT DETECTED**
3. **MTB DETECTED; Rif Resistance INDETERMINATE**
4. **MTB NOT DETECTED**
5. **Error**
6. **Invalid**
7. **No result**

Conclusive results include:

MTB NOT DETECTED, MTB DETECTED with Rif Resistance/ without Rif Resistance.

Statistical Analysis

"We conducted a statistical analysis of the data collected in our study to evaluate the diagnostic accuracy of CBNAAT in detecting Mycobacterium tuberculosis (M. tuberculosis), assess its performance, and compare it with other diagnostic methods."

Data Collection

A total of forty-five patients participated in the study. Each patient underwent a series of diagnostic tests, including CBNAAT, Ziehl-Neelsen staining, Mantoux test, chest X-ray, and CT scan. The diagnostic results from these tests were collected and classified as either positive or negative for M. tuberculosis.

"To evaluate the performance of CBNAAT, key metrics such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using the following formulas:

- **Sensitivity**: The proportion of true positive cases among all actual positive cases.
- **Specificity**: The proportion of true negative cases among all actual negative cases.
- **Positive Predictive Value (PPV)**: The probability that an individual with a positive test result actually has the disease.
- **Negative Predictive Value (NPV)**: The probability that an individual with a negative test result is truly free of the disease."

True positives (TP) were defined as patients with a positive CBNAAT result and confirmed **M. tuberculosis** infection through other diagnostic tests. False positives (FP) were patients with a positive CBNAAT result but negative confirmatory tests. True negatives (TN) were patients with negative CBNAAT results and no evidence of **M. tuberculosis** infection, and falsenegatives (FN) were patients who had a negative CBNAAT result but were confirmed to have **M. tuberculosis** through other tests.

Statistical Software and Significance Testing

Statistical analyses for this study were performed using SPSS software (Version 17), with a significance level set at $p < 0.05$. To compare the diagnostic performance of CBNAAT with other methods (Ziehl-Neelsen staining, FNA, and culture), a chi-square test was conducted for categorical variables. Additionally, the agreement between CBNAAT results and the gold standard diagnostic methods was assessed using Cohen's Kappa coefficient.

OBSERVATION AND RESULTS

OBSERVATION AND RESULTS

There were 45 suspected cases of Tuberculosis on whom GA CBNAAT was performed. Out of these, 37 tested negative for CBNAAT, while 8 tested positive.

Out of all patients with a negative GA CBNAAT result, BAL CBNAAT was performed to detect any more cases of confirmed TB.

Table 1: Age and sex of suspected TB cases

Age in Years	**Total suspected TB Case N=45**			**Cases where GA for CBNAAT –ve& BAL done n=37**			**Cases where GA for CBNAAT was positive n=8**		
	M	**F**	**Total**	**M**	**F**	**Total**	**M**	**F**	**Total**
0 to 3	2	1	3	2	0	2	0	1	1
03 to 07	1	2	3	2	1	3	0	0	0
07 to 11	6	4	10	4	2	6	2	2	4
11 to 15	6	13	19	6	11	17	0	2	2
15 to 18	2	8	10	1	8	9	1	0	1
Total	17	28	45	15	22	32	3	5	8
Mean Age (SD)			11.85 (4.25)			12.50(3.90)			8.75 (4.46)
Median age (IQR)			13(9-15)			13.75(11-15)			8.5 (5.5-10.25)

BAL was performed only in cases that were GA CBNAAT negative due to resource limitations. Patients who tested positive for GA CBNAAT were started on ATT, and BAL CBNAAT was not performed.

In the study, a total of 22 females and 15 males were included. The majority of cases were older than 12 years (26 out of 37, accounting for 70.27%). The youngest participant in the study was 3 years old. Mean age of all suspected TB patients was 11.85. There was

significant difference between the mean age of patients where GA CBNAAT negative (12.5 yrs.) and GA CBNAAT positive (8.75yrs) (P = 0.023).

There was a history of TB contact in 18 out of 37 study cases (45.94%). Among them, 11 were male, and 7 were female. Past history of tuberculosis was not present in any patient.

Table 2: Distribution of Living Areas among Study Cases

Living Areas	Number	Percentage
Urban	24	53.33
Rural	21	46.66

There were slightly more cases from urban area than rural area but the difference was not statistically different (p=0.712)

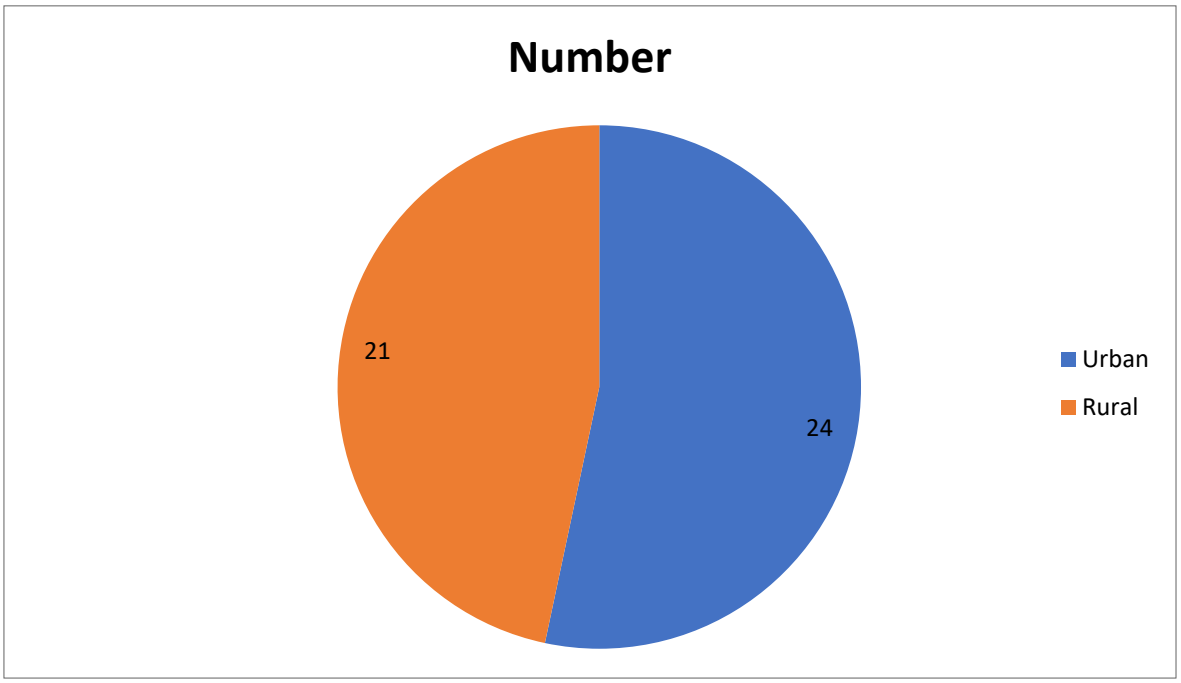

Fig 3. Rural and Urban distribution of suspected TB cases.

Table 3: Suspected Extra Pulmonary sites of TB

Extra Pulmonary TB sites	Total suspected TBcases		GA CBNAAT negative cases		GA CBNAAT Positive cases	
	Number	Percentage	Number	Percentage	Number	Percentage
Lymphadenopathy	5	11.11	5	13.51	0	0
CNS TB	1	2.22	1	2.70	0	0
Abdominal TB	2	4.44	2	5.40	0	0
Bone and Joint TB	1	2.22	1	2.70	0	0
None	36	80	28	28	8	100
Total	45	100	37	100	8	100

A total of 36 patients (80%) had only pulmonary TB, with no other sites affected. Out of these cases CBNAAT was positive in 8 cases. Among extrapulmonary TB cases, lymphadenopathy was the most common site, accounting for 13.51%.

BAL was done in 37 GA for CBNAAT negative cases.

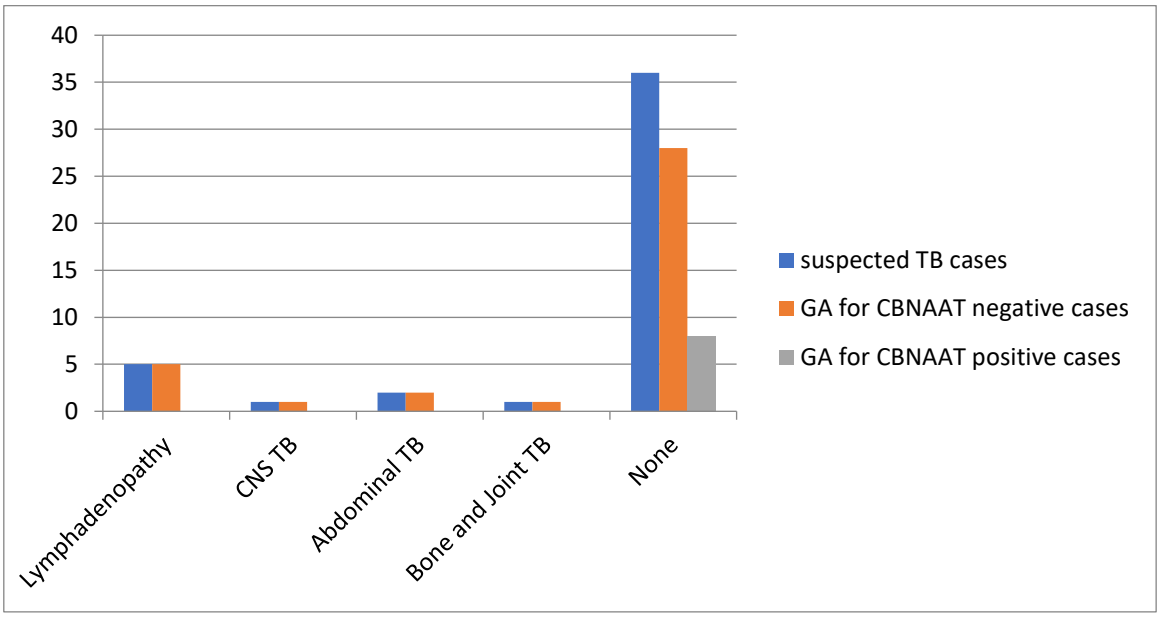

Fig 4- Extrapulmonary site of tuberculosis in addition to pulmonary TB

Table 4: Symptoms of suspected tuberculosis cases

Symptoms	In total Suspected TB Cases (N=45)	Percentage out of 45	GA CBNAAT negative cases (N=37)	Percentage out of 37	GA CBNAAT positive cases(N=8)	Percentage out of 8
Cough>2 wks.	39	86.66	33	89.18	6	75.00
Fever>2 wks.	38	84.44	33	89.18	5	62.50
Weight loss >5% in 3mths	30	66.66	27	72.97	5	62.50
Breathlessness	21	46.66	19	51.35	2	25.00
Hemoptysis	2	4.44	1	2.70	1	12.50
Pain Abdomen	3	8.10	3	8.10	0	0
Pain and swelling	1	2.22	1	2.70	0	0
Headache and Neck stiffness	1	2.22	1	2.70	0	0

Cough, fever, weight loss and breathlessness were the most common symptoms.

Table 5: Physical Examination findings

Physical Examination	Total Suspected cases (N=45)	Percentage out of 45	GA CBNAAT negative cases/ (N=37)	Percentage out of 37	GA CBNAAT positive cases (N=8)	Percentage out of 8
Tachypnea	23	51.11	21	56.75	2	25.00
Hypoxia (Saturation less than 95% on room air)	20	44.44	18	48.64	2	25.00
Chest in drawing	8	17.77	8	21.62	0	0
Lymphadenopathy	6	13.33	6	16.21	0	0
Pallor	11	24.44	8	21.62	3	37.50
Severe Thinness	10	22.22	6	16.21	4	50

Respiratory signs (tachypnea, hypoxia and desaturation) were present in more than half of the patients. Pallor and severe thinness were present in significant number of patients.

Table6: Mantoux Test Results

Mantoux test	Total Suspected case (N=45)	Percentage out of 45 (%)	GA CBNAAT negative cases/BAL Study Group(N=37)	Percentage Out of 37 (%)	GA CBNAAT positive cases(N=8)	Percentage out of 8 (%)
Positive	38	84.44	31	83.78	7	87.50
Negative	7	15.55	6	16.21	1	12.50
Not performed	0	0	0	0	0	0

Mantoux was done in all cases. There was no significant difference between the Mx positivity rate between GA CBNAAT negative cases and GA CBNAAT positive cases (p=1.000)

Table 7: Laboratory reports in all suspected cases of pulmonary tuberculosis) N=45)

Parameter	Mean + SD
Haemoglobin (g/dL)	11.34+ 1.73
Total Leukocyte Count (TLC) (cells/mm³)	10153.62+ 6313.11
Erythrocyte Sedimentation Rate (ESR) (mm/hr)	32.97+ 10.32
Platelet Count (×10³/µL)	322.33+ 122.95

Mean blood values were near normal except ESR which was high.

Table 8: Abnormal Lab Investigations

Parameter	Total suspected cases (N=45) N (Percentage)	GA CBNAAT negative cases (N=37) N (Percentage)	GA CBNAAT positive cases=8 N (Percentage)
Hemoglobin <10 (g/dL)	10 (22.22 %)	7 (18.91%)	3 (37.50%)
TLC<4000 (cells/mm^3)	0	0	0
TLC>14000 (cells/mm^3)	7 (15.55%)	5 (13.51 %)	2 (25%)
ESR>20 (mm/hr)	41 (91.11%)	36 (97.29%)	5 (62.50%)
Platelet Count<1.5 (×10^3/µL)	1 (2.22%)	1 (2.70%)	0
Platelet Count>4.5 (×10^3/µL)	9 (20%)	8 (21.62%)	1 (12.50%)

One third to one fourth numbers of patients had anemia, more in CBNAAT positive cases. ESR was high in most of the patients. Other parameters were deranged only in small number of patients.

Table 9: Radiological Signs in Subjects with Pulmonary TB

Radiological signs Pulmonary TB	Total suspected case (N=45)	Percentage out of 45	GA CBNAAT negative cases/BAL study group(N=37)	Percentage out of 37(%)	GA CBNAAT positive cases (N=8)	Percentage out of 8
Consolidation/ Collapse	18	40	16	43.24	2	25.00
Mediastinal Lymphadenopathy	7	15.55	6	16.21	1	12.50
Miliary TB	1	2.22	1	2.70	0	0
Fibrocavitatory lesion	9	20	5	13.51	4	50.00
Pleural effusion	6	13.33	5	13.51	1	12.50
Pericardial effusion	0	0	0	0	0	0

- Consolidation/Collapse was the most common radiological finding, observed in 40% of suspected cases and 43.24% of the BAL study group. All GA for CBNAAT negative cases had been subjected to BAL.
- Fibrocavitatory lesions and mediastinal lymphadenopathy were also frequently seen.
- No cases of pericardial effusion were reported.
- No patient had normal x-ray

Table 10: CECT Findings in Suspected TB Cases

CECT Scan	Total suspected case (N=18)	Percentage out 18 (%)
Consolidation/Collapse	13	72.22
Mediastinal Lymphadenopathy	3	16.66
Miliary	1	5.55
Fibrocavitatory lesion	1	5.55
Pleural effusion	2	11.11
Pericardial effusion	0	0

A CT scan was performed on 18 cases who were negative for GA for CBNAAT (37 cases) who were willing to undergo the investigation. The remaining 19 cases were advised to have a CT scan but did not undergo CT due to cost involved.

- Consolidation/Collapse was the most common finding, observed in 72.22%
- Miliary TB and fibro-cavitatory lesions were observed in 5.55% of suspected cases.
- No cases of pericardial effusion were reported in either group.
- CECT findings are valuable in detecting TB-related complications and assessing disease extent

Out of the total 45 suspected TB cases where GA CBNAAT was performed, 8 cases tested positive (17.7%) and were started on treatment without any further testing. The remaining 37 cases were negative for GA CBNAAT, and BAL CBNAAT was conducted for all 37 of them.

Table 11: Observation Results BAL CBNAAT

Observation	CB NAAT in BAL n -37	Percentage (%)
Detected	11	29.72
Not detected	26	70.27
Total	37	100

In those 37 cases GA for CBNAAT negative and BAL for CBNAAT done 11 (29.72% of BAL samples) more came out positive for BAL CBNAAT. It suggests that use of both tests cumulatively increases the yield of CBNAAT.

Table 12: Final diagnosis and stating ATT

	Total Suspected TB case	**GA CBNAAT + Ve**	**GA CBNAAT –Ve BAL CBNAAT +Ve**	**GA CBNAAT –Ve BAL CBNAAT-VE**
Total no of Cases	45	8	11	26
ATT Started	28	8	11	9

All patient where CBNAAT positive either on GA or on BAL started ATT. Additional 9 out of 26 patient who were CBNAAT negative for both GA and BAL were started ATT on strong clinical suspicion.

Table 13 –Final diagnosis of Patients in whom ATT was not started (n-17)

S No	Diagnosis	No of cases
1	Pneumonia	6
2	Infected scabies with Lymphadenopathy	1
3	Acute pain abdomen settled	3
4.	Pneumonia with synpneumonic pleural effusion	7

17 patients who were diagnosed as other than CBNAAT positive Pulmonary Tuberculosis were not started on ATT but improved on antibiotics and other supportive treatment. **(Table 13)**

In BAL study group 05 patients were positive for AFB smears on ZN stain. In these 05 patients BAL CBNAAT was also positive.

All of these results were negative for GA in the CBNAAT. The AFB smear was not tested on GA AFB, and no culture was performed in this study, either on BAL samples or GA samples. None of the patients experienced complications from the BAL procedure. In the 19 CBNAAT-positive cases, none showed resistance to Rifampicin. Of the patients in the study, 15 patients among the 45 required oxygen support via nasal prongs, and no patient required ventilation. All these patients were negative on GA for CBNAAT. AFB smear was not tested on GA AFB. Culture was not done in this study either on BAL sample or on GA sample.

DISCUSSION

DISCUSSION

The present study was a hospital based study on suspected cases of pulmonary tuberculosis with the aim to compare the detection rate of MTB with CBNAAT in Broncho-Alveolar Lavage (BAL) and Gastric Aspirate (GA) for the diagnosis of Tuberculosis in Pediatric age group. The main objectives were to detect Mycobacterium by CBNAAT in BAL fluid in patients who were having CBNAAT negative in GA. GA for CBNAAT was done in all 45 suspected cases. Since BAL is a specialized investigation requiring expertise and resources it was done only for those found to be CBNAAT negative on GA.

Diagnosing pulmonary tuberculosis in children is particularly challenging because of Paucibacillary nature with the disease and the difficulty in obtaining appropriate respiratory specimens. Traditional tests like sputum smear microscopy and culture have limited sensitivity in pediatric cases. Alternative specimens such as GA and BAL fluid are therefore utilized. CBNAAT has emerged as a rapid and reliable diagnostic tool, detecting MTB complex DNA and Rifampicin resistance within hours. The WHO policy update in 2017 for CBNAAT for the detection of pulmonary and extra-pulmonary TB in both adults and children has recommended that particularly in children, Xpert MTB/RIF may be done rather than usual microscopy and culture as the initial diagnostic test in all children suspected of having TB[61].NTEP guidelines emphasize exhausting all diagnostic options before initiating ATT, provided the clinical condition allows. CBNAAT is faster than culture and more sensitive than smear microscopy, enabling early ATT initiation. Additionally, detecting Rifampicin resistance ensures timely and appropriate treatment for drug-resistant TB cases.

In our study, 45 children were included between September 2023 to February 2025 with mean age of 11.85 yrs **(Table1).** There was a history of TB contact in 45.94% cases but past history of tuberculosis was not present in any patient. In a study by Sandip Sen et al,18%[7]children (less than 11yrs 3 months) with pulmonary tuberculosis had a history of TB contact. By Minakshi Johari et al **[11]** among 102 children 35.3% had a history of contact with someone who had TB. In yet another paediatric study positive history of contact was found in 33% **[10,11]**.

However, in a study, 08.39% of adult patients had history of contact with the TB patients and 46.85% of patients had previous history of tuberculosis.**[5]**None of the participants in this study

had a past history of tuberculosis, suggesting that all these patients were suffering from primary infections rather than reactivations.

Regarding residential distribution among suspected cases of TB, 24 cases (53.33%) were from urban areas; while 21 cases (46.66%) were from rural areas and the variation was not statistically significant (**Table2**).This indicates that TB is a concern in both urban and rural populations in our study area; necessitating region-specific diagnostic and preventive strategies.

An analysis of suspected extra-pulmonary TB cases showed that 36 patients (80%) had only pulmonary TB, with GA CBNAAT positivity detected in 8 of these cases. Among the extra-pulmonary TB sites with pulmonary TB, lymphadenopathy was common site, about 13.51% of suspected cases **(Table 3).** Other suspected extra-pulmonary TB sites included CNS TB (02.22%), abdominal TB (04.44%), and bone and joint TB (02.22%). However, none of these extra-pulmonary cases detected for Mycobacterium tuberculosis on GA CBNAAT. This further supports the notion that GA is more suitable for pulmonary TB detection and has limited utility in extra-pulmonary TB cases. Since BAL CBNAAT was only performed in GA-negative cases, its role in detecting extra-pulmonary TB was not extensively evaluated in this study. In an identical study by Singh KG [62]in Delhi observed that, among 50 individuals aged 0-14 years with having pulmonary tuberculosis (PTB), 23 (46%) were diagnosed with PTB using the RNTCP algorithm. Of the children in the PTB group, 16 (69.5%) were Xpert-positive, while none in the ‘not PTB' group tested positive by Xpert. When culture was used was the gold standard, the sensitivity and specificity of Xpert were 91.6% (95% CI 59.7–99.5) and 86.8% (95% CI 71.1–95.05), respectively. This clearly indicates that CBNAAT is superior to ZN smear for diagnosing pediatric tuberculosis. In the study by Singh M [63] CBNAAT was positive in 60 out of 449 smear-negative cases (13.4%) and also identified 10 cases of Rifampicin resistance among the 165 cases detected by CBNAAT (6.1%)[64].In Our study no resistance to rifampicin was detected.

The most common symptoms among the suspected TB cases were cough for more than two weeks (86.66%), fever persisting for over two weeks (84.44%), weight loss exceeding 5% in three months (66.66%), and breathlessness (46.66%), (**Table 4**). Some have minimal symptoms included Hemoptysis (04.44%), abdominal pain (08.10%),and headache with neck stiffness (02.22%). The higher prevalence of cough, fever, and loss of weight suggests that these symptoms should be prioritized when screening for pediatric TB, as they may serve as

early indicators of infection. In an adult studies, cough, fever and loss of weight and appetite were common symptoms [64]. By WHO the most presented signs and symptoms of childhood TB are chronic cough that has not subsided for 21 days, fever >38°C for 14 days, after other causes, including pneumonia, have been excluded, objectively presented weight loss or failure to thrive; feelings of having sickness or weakness, lethargy, and night sweats[65].

In this study Physical examination findings revealed that Tachypnea (51.11%) and hypoxia (44.44%) were the most frequently observed clinical signs. Other notable findings included lymphadenopathy (13.33%), pallor (24.44%), and severe thinness (22.22%), (**Table 5**). Pallor was more frequently observed in GA CBNAAT-positive cases (37.50%) compared to GA-negative cases (21.62%), suggesting that anemia may be associated with more advanced TB infection. Severe thinness, an indicator of malnutrition, was significantly higher in CBNAAT-positive cases (50%) compared to GA-negative cases (16.21%). This highlights the well-established link between malnutrition and TB, as under nutrition weakens immune defences and increases susceptibility to infection.

In the present study Mantoux test was positive in more than 80% cases in our study irrespective of GA CBNAAT positive or negative (**Table 6**). In a pediatric study by Sandip Sen et al [66], 16% tested positive for Mantoux. Variation in Mantoux positivity may depend on immunity of patients and correct technique used.

In the present study Among the 45 suspected TB cases, 10 (22.22%) had hemoglobin levels below 10 g/dL, with a higher proportion in GA CBNAAT-positive cases (37.50%**)** compared to the GA CBNAAT-negative/BAL study group (18.91%**),** (**Table7,8**)**.** No significant changes were found in TLC and platelets. An elevated erythrocyte sedimentation rate (ESR >20 mm/hr.) was present in 91.11% of total patients, being more repeated in the GA CBNAAT-negative group (97.29%**)** compared to GA CBNAAT-positive cases **(**62.50%**),** reinforcing the inflammatory nature of TB. Laboratory findings help to make diagnosis and assess the systemic impact of TB and guide clinical management.Dunn JJ et al [67]from their result found significant variation in WBC, neutrophil, and monocyte counts, and also in the Neutrophil to Lymphocyte, Monocyte to Lymphocyte and NMLR ratios when comparing community Acquired Pneumonia (CAP)and TB. They proposed that above parameters, which are strong indicators of acute inflammation; serve as useful and cost-effective laboratory markers for differentiating pulmonary TB from CAP in the previous stages of diagnosis. Basic, first-line laboratory results can be account in this context.

In this study among the 45 suspected pulmonary TB cases, radiological abnormalities were present in all patients, with consolidation or collapse being the most common finding, observed in18cases(40%), **(Table 9).** Fibro- cavitatory lesions were noted in 20% of cases, with a significantly higher occurrence in GA CBNAATpositive cases **(**50%**)** compared to GA CBNAATnegative cases (13.51%**).**Mediastinal lymphadenopathywas present in 15.55% of cases, while pleural effusion was observed in 13.33%**.**Miliary TBwas rare, detected in only one case (02.22%) from the GA CBNAAT-negative group. No cases of pericardial effusion were reported. Importantly, no patients had a normal chest X-ray**,** highlighting the significant radiological involvement in suspected pulmonary TB cases. In a study by Himanshu Singh Bisht et al [68]**,** they found that in view of radiological findings, one of the main observations was infiltration (71.90%), followed by consolidation (30.19%) in positive PTB cases. In an adult study on 43 patients pulmonary infiltrations were seen in 22 patients, consolidation in 12 patients, both consolidation and infiltrates in 02 patients, cavity with infiltrates in 04Patients, collapse with consolidation seen in 03 patients. In a study by Mohapatra G C,Bharti S **[69]**where consolidation was found in 33.3% and infiltration in 79% of patients, respectively.

In this study a contrast-enhanced computed tomography (CECT) scan was performed on18 out of 37suspectedTB cases that had GA for CBNAAT negative, as the remaining 19 patients declined the investigation due to cost constraints (Table 10). Among those who underwent CECT, consolidation or collapse was the most common radiological finding, observed in 72.22% of GACBNAAT-negative/BAL study group. Mediastinal lymphadenopathywas present in 16.66%.Miliary TB and fibro-cavitatory lesions were rare, each observed in 05.55% of cases. Pleural effusion was detected in 11.11%of cases who had GA for CBNAAT negative. These CECT findings highlight the utility of advanced imaging in detecting TB-related complications and assessing disease extent, especially in cases with inconclusive initial investigations. Buonsenso D et al **[70]**compared CECT and CXR in detecting pulmonary TB cases, based on the proposed radiological probability criteria, and they revealed that CT was superior in identifying probable TB images (70.3%) compared to 36.6% with X-ray. Additionally, they observed that 7 normal CXRs (17.1%) showed abnormalities on CT scans, with the difference being statistically significant ($p < 0.01$). Furthermore, pulmonary lymph-adenopathies were detected in 89.2% of CT scans (33/37), while only 36.6% (15/41) were identified in CXRs.

TB diagnosis in children continues to be a challenge due to many reasons, like Difficulty in getting appropriate samples, Paucibacillary disease, and relatively high incidence of extra-pulmonary TB[71].For pulmonary TB, sputum-induced or expectorated or gastric aspirate (GA)is the most important sample for laboratory testing [72]. Other alternative method for diagnosis may be laryngeal specimen like swabs, Bronchioalveolar Lavage, nasopharyngeal secretion, etc.

In children, GA showed superior diagnostic accuracy when samples of ES, IS, or NP are used [73].In our study 08/45 (17.7%) cases were positive for CBNAAT in GA. We had used only one GA sample and yield might have been more if 3 samples were used. According to reports, GA samples may have the highest (40-92%) detection rate. Positivity rates for other samples were from 4-43% for BAL, 24-30% for nasopharyngeal secretion, 27-63% for a laryngeal specimen like swab, and 20-30%when utilizing[74].In a study, GA, 21.4% were detected by Xpert assay, 8.57%were detected for AFB in smear microscopy, and 22.9% were detected to be culture positive[75]. Another study done in pediatric patients showed that in pulmonary samples, CBNAAT detected MTB in 21.4% sputum/induced sputum samples and in 33% gastric lavage/aspirate samples[37].Thus, GA and IS are significant samples for the diagnosis of pediatric pulmonary TB[75]. We had used single GA sample. Singh M et al [63]reported the usefulness of Gene Xpert in Detection of TB in pediatrics from North Indian medical colleges with good results in which out of 50 children (0-14 yrs.) 23 were diagnosed TB. The sensitivity and specificity were 84.6% and 86.4% respectively[73].In a pioneering Indian study, from different centers,4,600 pediatric presumptive pulmonary TB cases were enrolled, which diagnosed 590 (12.8%, CI 11.8–13.8) pediatric PTB cases. Overall, 10.4% (CI 9.5–11.2) of presumptive PTB cases were detected by Xpert MTB/RIF, in comparison to 4.8% (CI 4.2–5.4) smear-positive results[75]. In a pediatric study of cases of tuberculosis CB-NAAT detected 100% of smear positive cases[76]. In our study also 05 cases were smear positive in BAL and all these were detected for CBNAAT.

In a study the specificity, sensitivity, NPV, PPV, and accuracy of CBNAAT against MGIT were 94.4%,75.0%, 92.7%,80.0%, and 90.0% respectively for GA samples. The specificity, sensitivity, NPV, PPV, and accuracy of CBNAAT against MGIT were 96.6%,63.64%, 93.44%77.8%,, and 91.42% respectively for IS samples[77].

Another study found specificity, sensitivity, PPV and NPV of CB-NAAT in clinically diagnosed pulmonary TB cases, CB-NAAT demonstrated a Positive Predictive Value (PPV) of 100%, a Sensitivity of 60%, a Specificity of 100%, and a Negative Predictive Value (NPV) of 65.8%, resulting in an overall diagnostic accuracy of 80.2%. Among patients with clinically diagnosed tuberculosis, Mycobacterium tuberculosis culture was detected in 18.9% of cases, AFB smear in 12.1%, while CB-NAAT yielded a positivity rate of 55.4% cases[78]. Other studies also reported similar results. [79. 80]

Detjen AK, DiNardo ARet al [22]reviewed 15 studies that included 4,768 respiratory specimens from 3,640 children investigated for pulmonary tuberculosis. Among all the children assessed, culture tests were positive for tuberculosis in 12% (420 of 3,640), while Xpert was positive in 11% (406 of 3,640). When compared to culture, Xpert showed pooled sensitivities and specificities for tuberculosis detection of 62% (95% credible interval 51–73) and 98% (97–99), respectively, for expectorated or induced sputum samples. For samples from Gastric Lavage, Xpert's sensitivity and specificity were 66% (51–81) and 98% (96–99), respectively. Xpert's sensitivity was 36–44% higher than that of microscopy. In culture-negative children who started anti-tuberculosis therapy, Xpert's sensitivity for expectorated or induced sputum was 2% (1–3). The pooled sensitivity and specificity of Xpert for detecting rifampicin resistance were 86% (95% credible interval 53–98) and 98% (94–100), respectively.

Table 11 showed that among the 37 cases whereGA CBNAAT was negative and BAL CBNAAT was performed, additional11 cases (29.72%) tested positive for TB using BAL CBNAAT, while 26 cases (70.27%)remained negative. This highlighted the added diagnostic value of BAL CBNAAT in detecting TB cases that were missed by GA CBNAAT, reinforcing its role as a crucial follow-up investigation in suspected pulmonary TB cases. This is in contrast to study by Douglas L et al[24]which showed was no correlation between the age and yield of CBNAAT from GA and BAL did not increase the yield any further. In adult studies which used lower dose of lidocaine showed BAL to be superior to GA (600 mg vs. 200-320 mg). Amount of saline instilled, technical difficulty in children for doing BAL may affect results[81]. But in this paediatric study lidocaine 60 mg was used in 2 cases only using induced sputum, despite adequate sputum production. However, in the same group of patients mentioned above, bronchoalveolar lavage (BAL) yielded a significantly higher CBNAAT positivity rate of 62.8%.

A study [82]conducted on 50 children (aged 0–14 years) with suspected pulmonary tuberculosis (PTB) collected sputum/induced sputum and gastric lavage samples over two consecutive days. Bronchoalveolar lavage was performed when clinically indicated. Based on clinical, radiological, and microbiological findings, PTB was diagnosed in 23 out of 50 cases. When gastric lavage alone was used, the diagnostic yield was 11 cases (47.8%), while sputum (expectorated or induced) alone detected 12 cases (52.1%). The difference between the two methods was not statistically significant ($p = 1$). However, combining gastric aspirate and sputum increased the diagnostic yield to 69.5%, significantly higher than using either sample independently.

Among 11 children who were unable to expectorate, sputum induction was performed in this study. In this subset, the diagnostic yield of gastric lavage was 4/11 (36.36%), whereas induced sputum identified 05/11 (45.45%). Combining both methods further increased the yield to 7/11 (63.6%), representing a 27.2% improvement compared to using gastric lavage alone. These findings highlighted the importance of induced sputum as a valuable tool for enhancing microbiological detection of PTB in young children who cannot expectorate, emphasizing its routine use in such cases[82].

Table 12 showed that Among the 45 suspected TB cases, all 19 patients who tested CBNAAT-positive either on GA (8 cases)or BAL (11 cases) were started on anti-tubercular treatment(ATT). Additionally, 9 out of 26 patients who tested negative on both GA and BALCBNAAT were also initiated on ATT based on strong clinical suspicion. This underscores the importance of clinical judgment in TB diagnosis, as some patients may require treatment despite negative molecular test results.

Table 13 showed those17 patients that were not started on anti-tubercular treatment (ATT)as alternative final diagnoses was made and patient improved after antibiotics or other relevant treatment.

In the BAL study group, 05 patients were positive for AFB smears, and in all 05 cases, BALCBNAAT was also positive, confirming TB. In another pediatric study CB-NAAT detected 100% of smear positive cases Notably, all these cases had negative GA CBNAAT results. AFB smear was not tested on GA samples, and AFB culture was not performed on either GA or BAL samples.

Overall, in our study, CBNAAT was positive in 19 out of 45 suspected cases (42.2%), whereas AFB smear was positive in 5 out of 45 cases (11.11%). In a different study involving clinically diagnosed tuberculosis, Mycobacterium tuberculosis culture was positive in 18.9% of cases, AFB smears in 12.1%, while CBNAAT identified positive cases in 55.4%[104.] Another study examining 70 gastric aspirate (GA) samples found that 15 (21.4%) were positive by the Xpert assay, while 6 (8.57%) were positive for AFB.

In another study,[83] 16 out of 70 gastric aspirate (GA) samples were culture-positive (22.9%). In an adult study, 162 sputum smear-negative pulmonary tuberculosis suspects underwent fibrotic bronchoscopy. Samples for AFB smear, AFB culture, and CBNAAT were collected[74]. Of these, 88 cases (54.32%) were diagnosed with pulmonary tuberculosis. Among the 74 CBNAAT-positive cases, 65 (87.84%) were identified as rifampicin-sensitive, while 9 (12.16%) were found to be rifampicin-resistant.

There were no complications reported from the BAL procedure. Among the19 CBNAAT-positive cases, none showed resistance to Rifampicin, indicating drug-susceptible TB. Additionally, 15 cases required oxygen support via nasal prongs, but no patient required mechanical ventilation.

Implications and Future Directions

The findings reinforce the need for a structured diagnostic approach, where GA CBNAAT is the preferred initial test due to its non-invasive nature as children cannot easily expectorate and give sputum sample. In cases where GA is negative, BAL CBNAAT can be considered in resourceful settings to enhance case detection, especially in children with persistent clinical suspicion. While this study primarily focused on pulmonary TB, the presence of suspected extra-pulmonary TB cases underscores the need for additional diagnostic samples, such as fine needle aspiration cytology (FNAC), cerebrospinal fluid (CSF) analysis, and imaging studies, to improve extra-pulmonary TB detection.

Moreover, the high prevalence of malnutrition among CBNAATpositive cases underscores the importance of nutritional support as part of TB management. Programs such as the Ni-kshay Poshan Yojana, which provides direct benefit transfers for nutritional support to TB patients in India, should be strengthened to improve treatment outcomes.

Overall, this study highlights the diagnostic challenges in pediatric TB and the main part of integrating multiple testing strategies to improve case detection. Future research work should explore alternative, less invasive methods with comparable sensitivity to BAL CBNAAT, particularly for children in resource-limited settings. Additionally, larger studies evaluating the significant part of CBNAAT in extra-pulmonary TB cases are warranted to determine its overall effectiveness in pediatric TB diagnosis.

Strengths of our Study was prospective Study Design allowing for real-time data collection and minimizing recall bias, which enhances the accuracy and reliability of findings. Also, use of a Reliable Testing Laboratory for CBNAAT testing which was conducted in a certified and reliable laboratory, ensuring high-quality, standardized, and reproducible results, reducing the chances of diagnostic errors.

Weaknesses of the study were small sample Size and a single centre study. Tubercular culture was not performed which is the gold standard for TB diagnosis on either GA or BAL samples. This limits the ability to compare the results of CBNAAT with gold standard. Single GA Sample was tested per patient, whereas 3 GA samples might have increased TB detection rates. Selective BAL Testing was performed only in GA CBNAAT negative cases, because of which yield from GA and BAL could not be compared.

CONCLUSIONS: We can conclude that the study provided significant insights into TB diagnosis. In GA for CBNAAT negative cases BAL can detect more CBNAAT positive cases if resources are available to do this test. Therefore, GA and BAL complement given each other to increase the diagnostic yield.

Limitations were that this study had small sample size, absence of culture testing, reliance on a single GA sample, and selective BAL testing highlight the need for further research work with expanded diagnostic protocols in larger number of patients.

CONCLUSION AND RECOMMENDATIONS

CONCLUSION

This study evaluated the diagnostic utility of CBNAAT in gastric aspirate (GA) and bronchoalveolar lavage (BAL) samples for suspected tuberculosis (TB) cases in a hospital setting. The findings indicate that while GA CBNAAT is a valuable initial diagnostic tool, BAL CBNAAT plays a crucial role in detecting TB in cases where GA results are negative. The additional testing with BAL CBNAAT led to an increase in TB detection rates, suggesting its importance in diagnosing difficult-to-confirm cases.

The study also highlights the need for a more comprehensive diagnostic approach for TB, particularly in patients with negative GA CBNAAT results but strong clinical suspicion of the disease. However, limitations such as sample size and potential selection bias should be acknowledged. Future studies with larger cohorts and comparative analyses with other diagnostic methods could further validate these findings.

Furthermore, this study underscores the necessity of integrating multiple diagnostic tools to enhance the accuracy of TB detection. The role of BAL CBNAAT in diagnosing Pauci bacillary and smear-negative TB cases should be further explored. The study also indicates the potential for improved patient outcomes when an aggressive diagnostic approach is taken, leading to earlier initiation of treatment and reduced disease progression. Additionally, cost-effectiveness analyses of incorporating BAL CBNAAT into routine practice should be considered to determine its feasibility in resource-limited settings.

RECOMMENDATIONS

1. Clinical Practice: BAL CBNAAT should be considered a supplementary diagnostic test in patients with negative GA CBNAAT results but persistent clinical and radiological suspicion of TB.

2. Diagnostic Protocols: Hospitals should consider revising TB diagnostic protocols to include BAL CBNAAT as a standard secondary test when GA CBNAAT results are inconclusive.

3. Further Research: Additional studies with larger sample sizes and multi-center collaborations should be conducted to confirm the reliability of BAL CBNAAT and compare it with other diagnostic modalities.

4. Public Health Impact: Early and accurate TB detection using a combination of GA and BAL CBNAAT can lead to timely treatment initiation, reducing disease transmission and improving patient outcomes.

5. Training and Awareness: Healthcare professionals should receive training on the utility of BAL CBNAAT to ensure its effective implementation in clinical settings.

6. Integration of Diagnostic Tools: A multi-modal diagnostic strategy incorporating CBNAAT with other molecular and imaging techniques should be explored to improve overall TB detection rates.

7. Cost-effectiveness Analysis: Further evaluation of the economic feasibility of implementing BAL CBNAAT in different healthcare settings should be conducted to guide policymakers in resource allocation.

8. Policy Implications: Government and health agencies should consider updating TB diagnostic guidelines to reflect emerging evidence supporting the use of BAL CBNAAT in difficult cases.

SUMMARY

SUMMARY

Tuberculosis (TB) remains a significant global health challenge, in terms of both mortality and morbidity. In 2020, approximately 10 million people were affected by TB worldwide, including 1.1 million children. Around two-thirds of all TB cases were concentrated in just eight countries, with India bearing the largest burden. In 2023, an estimated 10.8 million individuals fell ill with TB globally. In India, the rate of microbiologically confirmed pulmonary tuberculosis in individuals aged 15 and older was 316 cases per 100,000 people in 2022.

Untreated mortality rate of tuberculosis is approximately 50%, but cure can be achieved by comprehensive anti-tubercular therapy in about 85% of individuals who do not have rifampicin resistance.

Diagnosis can be made in suspected cases of TB by direct visualization of acid-fast bacilli (AFB) in smear or culture or by nucleic acid amplification techniques (NAAT). Indirect diagnosis can be made in patients with suggestive history and signs based on tuberculin skin test, radiology, blood counts, erythrocyte sedimentation rate (ESR), or adenosine de aminase (ADA) levels.

Improving the efficiency and accuracy of TB diagnosis contributes to treatment efficacy. Despite over a century since Robert Koch discovered tubercle bacilli in 1882, TB remains a challenging disease to diagnose. Radiological imaging, such as chest X-rays, is a valuable tool but lacks specificity. In children, perihilar or paratracheal lymphadenopathy is a hallmark, though findings on high-resolution computed tomography (HRCT) may be more revealing than standard X-rays.

Microscopic examination of sputum smears using Ziehl-Neelsen (ZN) staining has been used for over a century. While inexpensive and specific, it lacks sensitivity and is operator-dependent. Culture remains the gold standard, but it is time-consuming, taking up to 25 days for solid media and two weeks for liquid media. Practical use of culture methods is often limited in resource-constrained settings.

The World Health Organization (WHO) endorsed the CBNAAT (Cartridge-Based Nucleic Acid Amplification Test) for rapid TB diagnosis in 2010. India's Revised National

Tuberculosis Control Programme (RNTCP) has since incorporated CBNAAT at district and sub-district levels. The GeneXpert MTB/RIF system allows rapid detection of TB and rifampicin resistance within two hours. CBNAAT has a lower detection threshold than smear microscopy and culture, making it a valuable tool for early diagnosis.

Diagnosing TB in children remains challenging due to the Pauci bacillary nature of the disease and difficulty in obtaining appropriate samples. Sputum is the preferred sample, but young children often cannot expectorate, leading to the use of gastric aspirate (GA) and bronchoalveolar lavage (BAL). Studies suggest that GA has a high TB detection rate (40-92%), whereas BAL detection rates vary from 4-43%. Some studies indicate that BAL does not significantly increase diagnostic yield over GA, while others show that BAL is more effective, especially in adult patients.

Given the lack of extensive studies comparing GA and BAL CBNAAT efficacy in pediatric patients, this study aims to determine whether BAL CBNAAT improves TB detection in suspected cases with negative GA CBNAAT results.

Aim To compare the positivity of detection of **Mycobacterium tuberculosis** with CBNAAT in BAL fluid and Gastric Aspirate to diagnose pulmonary tuberculosis in the pediatric age group.

Objectives

- To detect **Mycobacterium tuberculosis** in BAL fluid using CBNAAT.
- To detect **Mycobacterium tuberculosis** in gastric aspirate using CBNAAT.
- To compare the diagnostic yield from BAL fluid and gastric aspirate CBNAAT.

Methodology

- Study Design: Hospital-based observational study.
- Study Setting: Pediatric Department, Santosh Medical College and Hospital, Ghaziabad, Uttar Pradesh.

- Study Population: Clinically suspected cases of pulmonary tuberculosis, both inpatient and outpatient, enrolled after obtaining consent.
- Study Duration:1 year
- Sample Size: 45 patients, divided into two groups based on the sample material (BAL group and Gastric Lavage group).
- Procedure:
    - GA samples were initially tested using CBNAAT, and if results were negative, BAL samples were collected for further CBNAAT testing.
    - The data was analyzed, and the results were compared between the two groups.
- Statistical Analysis: The sample size was calculated using sensitivity and specificity estimations based on Wan NorAriffin's formula.

Key Findings

- GA CBNAAT is an effective primary diagnostic tool but has limitations in certain cases.
- BAL CBNAAT significantly improved TB detection in patients with negative GA results.
- A multi-modal diagnostic approach enhances early diagnosis and timely treatment initiation.
- The integration of BAL CBNAAT into diagnostic protocols can lead to better patient outcomes and reduced disease transmission.
- Further research is needed to determine the cost-effectiveness of widespread BAL CBNAAT implementation.

Conclusion: This study evaluated the diagnostic utility of CBNAAT in gastric aspirate (GA) and bronchoalveolar lavage (BAL) samples for suspected tuberculosis (TB) cases in a hospital setting. The findings indicate that while GA CBNAAT is a valuable initial diagnostic tool, BAL CBNAAT plays a crucial role in detecting TB in cases where GA results are negative. The additional testing with BAL CBNAAT led to an increase in TB detection rates, suggesting its importance in diagnosing difficult-to-confirm cases.

The study also highlights the need for a more comprehensive diagnostic approach for TB, particularly in patients with negative GA CBNAAT results but strong clinical suspicion of the disease. However, limitations such as sample size and potential selection bias should be acknowledged. Future studies with larger cohorts and comparative analyses with other diagnostic methods could further validate these findings.

Furthermore, this study underscores the necessity of integrating multiple diagnostic tools to enhance the accuracy of TB detection. The role of BAL CBNAAT in diagnosing Pauci bacillary and smear-negative TB cases should be further explored. The study also indicates the potential for improved patient outcomes when an aggressive diagnostic approach is taken, leading to earlier initiation of treatment and reduced disease progression. Additionally, cost-effectiveness analyses of incorporating BAL CBNAAT into routine practice should be considered to determine its feasibility in resource-limited settings.

Recommendations

1. Clinical Practice: BAL CBNAAT should be considered a supplementary diagnostic test in patients with negative GA CBNAAT results but persistent clinical and radiological suspicion of TB.

2. Diagnostic Protocols: Hospitals should consider revising TB diagnostic protocols to include BAL CBNAAT as a standard secondary test when GA CBNAAT results are inconclusive.

3. Further Research: Additional studies with larger sample sizes and multi-center collaborations should be conducted to confirm the reliability of BAL CBNAAT and compare it with other diagnostic modalities.

4. Public Health Impact: Early and accurate TB detection using a combination of GA and BAL CBNAAT can lead to timely treatment initiation, reducing disease transmission and improving patient outcomes.

5. Training and Awareness: Healthcare professionals should receive training on the utility of BAL CBNAAT to ensure its effective implementation in clinical settings.

6. Integration of Diagnostic Tools: A multi-modal diagnostic strategy incorporating CBNAAT with other molecular and imaging techniques should be explored to improve overall TB detection rates.

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9. Policy Implications: Government and health agencies should consider updating TB diagnostic guidelines to reflect emerging evidence supporting the use of BAL CBNAAT in difficult cases.

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ANNEXURES

PATIENT INFORMATION SHEET

(ANNEXURE 1)

NAME:

AGE:

ADDRESS:

REGISTRATION NUMBER:

CLASS/STUDY:

PHONE NUMBER:

CHIEF COMPLAINT

CASE PERFORMA

(ANNEXURE 2)

Name: Age: Regn. No.

Education Occupation

Address

Tel./ Mob. No.

CLINICAL DETAILS

Complaints :

Medical/ Surgical History :

FIRST VISIT

PHYSICAL EXAMINATION:

Temp	PR	BP
Pallor	Icterus	Cynosis
Clubbing	Lymphadenopathy	
Edema	Height Wt	

Respiratory System

CVS

CNS

SAMPLE FROM THE RESPECTIVE SITE:

GASTRIC ASPIRATE CBNAAT

BAL FLUID CBNAAT

DIAGNOSIS:

TREATMENT:

CONSENT FOR IN ENGLISH

(ANNEXURE 3)

INFORMED CONSENT

Name of the patient: Age:

Address: Phone Number:

S.NO: Date:

I have been explained the details of the study entitled **"COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS IN PEDIATRIC AGE GROUP"**and my questions regarding the study have been answered to my satisfaction in a language understood by me.

1. I understand that I have the right to withdraw from the study at anytime and to decline to answer any particular question.
2. I understand that my participation in this study is confidential and that no material that could identify me will be used in the analysis and in any reports based on this study.

I hereby provide my consent in the study entitled **"COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSISIN PEDIATRIC AGE GROUP"**

Signature/ thumb impression of the patient

Signature/ thumb impression of witness

CONSENT FORM IN HINDI (ANNEXURE 4)

सहभागी सुचित सहमति प्रपत्र

गाइड का नाम: -

रोगी का नाम: **आयु:**

पता: -

फ़ोन नंबर:-

एस एन ओ:

मुझे अध्ययन के विवरण समझाया गया है "COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSISIN PEDIATRIC AGE GROUP " मेरा अध्ययन के बारे में प्रश्नों को एक मेरे द्वारा समझा भाषा में मेरी संतुष्टि का उत्तर दिया गया

1. मैं समझता हूं कि मुझे किसी भी समय अध्ययन सेवा लेने का अधिकार है और किसी विशेष प्रश्न का उत्तर देने में गिरावट आई है।

2. मैं समझता हूं कि इस अध्ययन में मेरी भागी दारी गोपनीय है और सामग्री जो मुझे पहचान सकती है और रिपोर्ट इस अध्ययन के आधार पर किसी भी में विश्लेषण उपयोग नहीं की जाएगी। मैं इस प्रकार अध्ययन में अपनी सहमति प्रदान करता हूं "COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSISIN PEDIATRIC AGE GROUP"

रोगी के हस्ताक्षर / अंगूठे की छाप

गवाह के हस्ताक्षर / अंगूठे की छाप

ETHICAL CLEARANCE LETTER(ANNEXURE5)

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

F. No. SU/R/2023/2489[31] Dated: 26.09.2023

Subject: Grant of Ethical Clearance for **Thesis Protocol** Topic **"COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS IN PEDIATRIC AGE GROUP",** submitted by **Dr. HASHIM C,** MD/MS student of Batch 2022-2023, Department of **PAEDIATRICS.**

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS IN PEDIATRIC AGE GROUP", Dr. HASHIM C** is informed that the **Thesis Protocol** submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 17.07.2023 to 28.07.2023. The recommendations of the **Screening Committee** were considered in detail by the **Institutional Ethics Committee** in its meeting held on **23.09.2023** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. NARESH SHARMA]
REGISTRAR

SANTOSH DEEMED TO BE UNIVERSITY REGISTRAR GHAZIABAD, NEW DELHI

Dr. HASHIM C
MD/MS student of batch 2022-2023
Department of PAEDIATRICS
Email: drhashimchemban@gmail.com

Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Academics
4. The Dean – Research
5. The Director - IQAC
6. Dr. DK Juneja (Guide)
7. HOD of PAEDIATRICS

PLAGIARISM REPORT (ANNEXURE6)

Dr.Hashim C

COMPARATIVE STUDY OF CBNAAT IN BRONCHOALVEOLAR LAVAGE FLUID AND GASTRIC ASPIRATE FOR DIAGNOSIS OF...

Santosh University, Ghaziabad

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Workshop on Dissertation Writing

16th February 2025

Certificate Of Participation

Is presented to Dr Hashim C

For his/her participation as a faculty/ delegate/ in

Workshop on Dissertation Writing

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Ghaziabad (Delhi NCR).

Dr Alka Agarwal
Dean and Professor, SMCH Ghaziabad

Mahalakshmi
Dr. Mahalakshmi, V.N
Vice Chancellor

KEY TO MASTER CHART

(ANNEXURE 7)

1).Name- Name of the patients participated in the study.

2).Registration Number – IP Number /OP Number of the client participated in the study.

3).Age – Value in years.

4).Sex – Patient gender who participated in study

(1)- Represent for male

(2)-Represent for female

5).TB Contact – (1)- Represents positive for TB contact.

(2)- Represent negative for TB contact.

6).Urban/Rural – (1) – Belongs individual from Urban area.

(2) – Belongs individual from Rural area.

7).Weight in (KG)- Value of the weight of the individual in kilograms.

8).Height in (cm) – Value of Height of the individual in centimeters who participated in the study.

9).BMI (KG/m^2) - Value of body mass index of the individual in kilogram per metre square.

10).Cough > 2 weeks- (1) – Individual positive for cough more than two weeks.

(2) – Individual negative for cough more ths two weeks.

11).Fever > 2 weeks - (1) – Individual positive for having fever for more than two weeks

(2) - Individual negative for fever more than two weeks

12).Breathlessness - (1) - Individual having breathless positive

(2) – Individual not having breathless

13).Weight loss > 5 % -(1) Individual having weight loss more than 5 % in last 3 months – Positive .

- (2) Individual not having weight loss more tha 5 % in last 3 months- Negative .

14).Hemoptysis – (1)-Individual having hemoptysis represent .

-(2)-Individual not having hemoptysis .

15).Pain Abdomen – (1)-Having pain abdomen .

- (2)-Not having pain abdomen .

16).Tachypnea - (1) Individual having Tachypnea.

-(2) Individual not having Tachypnea .

17).Saturation < 95% on Room air- (1) Individual having Tachypnea .

-(2) Not having Tachypnea.

18).Chest wall retraction – (1)-Individual having abnormal chest wall retraction Positive .

(2) -Negative .

19).Oxygen support- (1) Patient kept under oxygen support .

(2)- Not having oxygen support and kept in room air .

20).Pallor – (1)-patient were hemoglobin less than 10 gm/dL represent .

- (2) having no pallor.

21).ESR in mm/hr- Value of ESR in mm per hour

22).Raised ESR (> 20 mm/hr)- (1) Patient whose ESR more than 20 mm/hr represents .

-(2) Patients whose ESR less than 20 mm/hr represents .

23).Hb in gm/dL – Value of hemoglobin in gm/dL

24).Hb Less than 10 gm/dL- (1) patient whose Hb less than 10 gm/dL .

-(2)-Hb more than 10 gm/dL represents.

25).TLC- Value of total count in cells/mm^3.

26).Platelets – Value of total count in ($\times 10^3/\mu L$)

27).X ray- Finding in X ray of the patients in study group

28).CT scan- Finding in the CT scan who underwent scanning among study group.

29).ZN stain-(1) Patient who undergone ZN staining and come to positive .

-(2)Who came negative.

-(3)Whom were ZN stain not performed.

30) GA CBNAAT – Individual who was detected for CBNAAT was (1)

-Who was not detected (2)

-whose test GA CBNAAT not performed was (3)

31).BAL CBNAAT- (1) Individual who was detected for BAL CBNAAT.

-(2)Who was not detected for BAL CBNAAT represents.

32). Rifampicin Resistance- (1) Individual who tested for Rifampicin resistance positive.-(2)Who was tested negative for Rifampicin resistance negative.

MASTER CHART (ANNEXURE 8)

No.	Name	Registration Number	Age	Sex	TB contact	Urban / Rural	Weight (in kG)	Height (in cm)	BMI (KG/m2)	cough >2 weeks	Fever >2 weeks	Breathlessness	Weight loss more than 5%	Hemoptysis	Pain Abdomen	Tachypnea	Saturation <95% ON ROOM AIR-2	Chest wall retraction	Oxygyen support	Pallor	ESR (mm/hr)	Raised ESR {>20 (mm/hr)}	Hb (g/dL)	Hb less than 10 (g/dL)	TLC (cells/mm³)	Platelets (×10³/µL)	X-Ray	CT scan	ZN Stain	GA CBNAAT	BAL CBNAAT	Rifampicin resistance	ATT started	Monteux Test
1	Soni	46041	15.8	2	2	1	44.5	158	17.8	1	1	1	1	2	2	2	2	2	2	2	32	1	10.6	2	8600	205	Collapse left lower lobe	consolidation Left lower Lobe	1	2	1	2	1	1
2	Aahil	50860	5	1	2	1	15.3	112	12.2	1	2	1	1	2	2	1	1	1	1	2	22	1	10.5	2	6240	296	Consolidation Right mid zone	Not done	2	2	2	2	2	1
3	Ikra	51461	12.8	2	2	2	22.8	150	10.1	2	1	1	1	2	2	1	1	2	1	1	42	1	8.9	1	9130	469	Pleural Effusion Right side	Not done	2	2	2	2	2	1
4	Mantasa	57112	16	2	2	2	40.3	161	15.5	1	2	2	2	2	1	2	2	2	2	2	28	1	11.2	2	4590	402	Opacity Left midzone with mediastinal glands	consolidation Left lower Lobe	2	2	2	2	2	1
5	Aysha	57546	15	2	1	1	43	158	17.2	1	1	1	1	2	2	1	1	2	1	2	45	1	13.5	2	5600	263	Collapse left lower lobe	Not done	1	2	1	2	1	1
6	Astha	57726	12	2	2	1	35	152	15.1	1	1	2	2	2	2	2	2	2	2	2	19	2	12.8	2	5220	201	Consolidation Right mid zone	Not done	2	2	2	2	2	2
7	Navya	100000	13	2	1	1	39	153	16.7	1	1	2	1	2	2	2	2	2	2	1	44	1	10.5	2	1902 0	546	Pneumonitis Left lower zone	Consolidtion Left lower lobes	2	2	2	2	1	1
8	Chhavi	50576	15	2	2	2	42	157	17	1	2	2	2	2	2	2	2	2	2	2	22	1	10.8	2	7450	256	Left side Pleural effusion	Not done	2	2	2	2	2	2
9	Manshi	51620	17.8	2	2	2	28.5	160	11.1	1	1	1	1	2	2	1	1	1	1	2	38	1	10.5	2	4431 0	705	Consolidation left lower lobe	Consolidtion Left lower lobes	1	2	1	2	1	1
10	Himanshu	59379	8	1	1	1	24	120	16.7	1	1	1	2	2	2	2	2	2	2	2	34	1	13.4	2	8070	510	Mediastinal glands Right side	not done	3	2	2	2	2	2
11	Priya Kumari	61972	15	2	1	1	38	156	15.6	1	1	1	1	2	2	1	1	2	1	1	48	1	9.8	1	6840	298	Pneumonitis Left lower zone	Not done	2	2	1	2	1	1
12	Siryansh	174389 64	3	1	1	2	12	88	15.5	1	1	2	1	2	2	2	2	2	2	2	28	1	11.9	2	7850	315	Opacity Left midzone with mediastinal glands	Not done	2	2	2	2	2	1
13	Shivani	59961	15	2	2	1	46	157	18.7	1	1	2	1	2	2	2	2	2	2	2	52	1	10.5	2	5290	375	Mediastinal glands Left side	consolidation left upper lobe	2	2	1	2	1	1
14	Avani Sharma	55027	12	2	2	1	22.9	151	10	1	1	1	1	2	2	1	1	2	1	2	28	1	13.1	2	1014 0	343	Collapse left lower lobe	Not done	2	2	2	2	1	1
15	Dheeraj	55513	14	1	1	1	33	155	13.7	1	1	2	1	2	2	2	2	2	2	2	44	1	11.5	2	6630	289	Mediastinal glands Right side	Not done	1	2	1	2	1	1
16	Mohit Bhardwaj	55833	13.8	1	1	2	55	156	22.6	1	1	2	2	1	2	1	2	2	2	2	32	1	16.3	2	4670	91	Opacity Left midzone with mediastinal glands	Not done	2	2	2	2	1	1
17	Neha	55904	16	2	2	1	43.6	163	16.4	1	2	2	1	2	2	2	2	2	2	2	28	1	12.5	2	9720	235	Pneumonitis Left lower zone	Consolidation Left lower zone	1	2	2	2	2	2
18	Jyoti	56669	17.8	2	1	2	36	162	13.7	2	1	1	1	2	2	1	1	1	1	1	33	1	9.3	1	5840	151	Collapse left lower lobe	Collapse Left lower lobe	2	2	2	2	2	1
19	Varsha	101577	14	2	1	2	42	156	17.3	1	1	2	2	2	2	1	1	1	1	2	28	1	12.6	2	1273 0	300	Pleural Effusion left side	collapse Left lower lobe	2	2	2	2	2	1
20	Himanshu	58756	3	1	1	2	12.2	88	15.8	1	1	1	2	2	2	1	1	1	1	2	36	1	13.4	2	9070	510	Opacity Left midzone with mediastinal glands	thick walled cavity left upper lobe- Suggestive TB	2	2	2	2	1	1
21	priyal	62600	7.75	2	2	1	19.4	123	12.8	2	1	1	1	2	2	1	1	1	1	1	27	1	9.9	1	8940	293	Consolidation Right mid zone	Not done	2	2	2	2	2	1
22	Vishal	62781	9.25	1	1	1	20.5	129	12.3	1	1	1	1	2	2	1	1	2	1	2	38	1	14.2	2	1225 0	195	Mediastinal glands Right side	Not done	2	2	1	2	1	1
23	Deepak	62969	12.5	1	1	2	26	148	11.9	1	1	2	1	2	2	1	1	2	1	2	39	1	10.5	2	8890	520	Opacity Left upper zone with mediastinal glands	consolidation left upper lobe	2	2	2	2	1	1
24	Bhanu Pratap Singh	63500	6	1	2	1	20	112	15.9	1	1	1	2	2	2	2	2	2	2	2	62	1	10.7	2	1650 0	423	Collapse right lower lobe	Empyema on right side with lung consolidation	2	2	2	2	2	1

25	Radhika	63479	14.5	2	2	2	35.4	158	14.2	1	1	2	2	2	2	1	1	1	1	2	46	1	11.9	2	15800	309	Consolidation right lower zone	collapse right lower lobe and consolidation right upper lobe	2	2	1	2	1	1
26	Karan	64211	13	1	1	2	26.8	151	11.8	1	1	2	1	2	2	2	2	2	2	2	52	1	10.2	2	9290	340	Miliary Nodule	Not done	3	2	1	2	1	1
27	Danib	64712	11	1	2	1	25.7	140	13.1	1	1	2	1	2	2	2	2	2	2	2	28	1	14	2	8560	305	Collapse left lower lobe	Not done	2	2	2	2	2	1
28	Inaya	65022	12	2	2	1	32	145	15.2	1	1	1	2	2	1	1	2	2	2	2	42	1	12.6	2	14590	258	consolidation left lower zone	Not done	2	2	2	2	2	2
29	Saniya	65132	15.3	2	2	2	54.5	159	21.6	2	1	1	2	2	2	2	2	2	2	1	32	1	8.2	1	6820	152	Pleural effusion right side	Not done	3	2	2	2	2	1
30	Mayank	65472	16	1	1	1	42	160	16.4	1	1	2	1	2	2	1	1	2	2	2	36	1	11.9	2	4830	220	Pneumonitis Left lower zone	Consolidation Left lower zone	2	2	2	2	1	1
31	Rohan	66003	14	1	2	2	44	152	19	1	1	2	2	2	2	2	2	2	2	2	22	1	11.5	2	9880	276	Consolidation Right Lower zone	Not done	2	2	2	2	2	2
32	Karthik	68074	12	1	1	2	30.6	149	13.8	1	1	2	1	2	2	1	2	2	2	2	18	1	12.5	2	6320	307	consolidation left lower zone	Not done	3	2	2	2	2	1
33	Saurabh kumar	73269	8	1	1	1	18.7	126	11.8	1	1	1	1	2	2	1	1	2	2	2	30	1	10.5	2	10390	496	Mediastinal glands Right side	Not done	2	2	1	2	1	1
34	Bharti	77932	16	2	1	2	46	158	18.4	1	1	2	1	2	2	1	1	2	2	2	38	1	11.2	2	6900	220	Consolidation right lower lobe	consolidation right lower lobe	3	2	1	2	1	1
35	Afiya	78417	9.25	2	2	1	20	132	11.5	1	1	1	1	2	2	2	2	2	2	1	42	1	9.4	1	12870	285	Mediastinitis Right mid zone	normal study	2	2	2	2	1	1
36	Teena Rani	80035	18	2	1	1	33.5	161	12.9	1	1	1	1	2	2	1	1	1	1	1	38	1	7.8	1	4660	464	Pleural effusion right side	right sided pleural effusion	2	2	2	2	1	1
37	Chanchal	82879	15	2	1	1	59	157	23.9	1	1	1	1	2	1	1	1	2	2	2	28	1	10	2	6057	239	consolidation with mediastinal glands right	tubercular abscess in thorax and pelvis	2	2	2	2	1	1
38	Kanishka	98208	4	2	1	2	17	98	17.7	2	1	1	2	2	2	1	1	2	1	1	19	2	9.7	1	18600	494	Opacity Right lower zone	Not done	3	1	3	2	1	2
39	Sarika	98282	14	2	1	1	41	155	17.1	1	2	1	1	1	2	2	2	2	2	2	21	1	11.2	2	11310	275	Consolidation Right Upper lobe	consolidation right upper lobe	3	1	3	2	1	1
40	Hussain	17397154	9	1	1	2	38	132	21.8	1	1	2	1	2	2	2	2	2	2	2	22	1	12.8	2	9620	232	Mediastinal glands right side	Not done	3	1	3	2	1	1
41	Imsha	105797	9	2	1	1	26	128	15.9	2	1	2	2	2	2	2	2	2	2	2	18	2	10.8	2	8640	225	Opacity Right lower zone	Not done	3	1	3	2	1	1
42	Charvi	107989	8	2	2	2	24.5	125	15.7	1	2	2	1	2	2	2	2	2	2	1	34	1	9.6	1	11650	376	Pleural Effusion left side	Not done	3	1	3	2	1	1
43	Arman	105011	17	1	1	2	46.9	162	17.9	1	1	2	2	2	2	2	2	2	2	2	18	2	14.6	2	8436	246	Opacity right midzone with mediastinal glands	Not done	3	1	3	2	1	1
44	Ananya	107129	3	2	1	1	11.1	92	13.1	1	2	2	1	2	2	1	1	2	1	2	29	1	11.1	2	13800	223	Opacity left midzone	Not done	3	1	3	2	1	1
45	Vaibhavi	17408357	6	2	1	2	15	106	13.3	1	1	2	1	2	2	2	2	2	2	1	22	1	9.9	1	14300	372	Consolidation left lower zone	Not done	3	1	3	2	1	1

ANNEXURE 9

REPORTING PROFORMA FOR CBNAAT RESULTS

The results for Nucleic Acid Amplification Test (NAAT) assays are entered in Culture and Drug Susceptibility Testing (C&DST) register. The key variables entered are shown in the table below.

Table: Key Variables entered in C&DST Register; Source: Guidelines for PMDT in India, 2021.

VARIABLES SET 1	VARIABLES SET 2	VARIABLES SET 3	VARIABLES SET 4
Test ID	Health Facility (HF) name	Residential district	Current facility HF type
Date of test updated in Nikshay	Lab type	Type of test	Predominant symptom
Date tested	Patient ID	Reason for testing	Predominant symptom duration
Date reported	Episode ID	Treatment status	History of Anti-TB Treatment (ATT)
Test status	Name	Diagnosis date	No. of Health Care Provider (HCP) visited before the diagnosis of the current episode

CRITERIA FOR ORDERING RE-TEST OF CBNAAT

(ANNEXURE 10)

Retest Procedure for CBNAAT

The assay needs to be repeated by using a new cartridge if one of the following test results occur:

INVALID: An INVALID result indicates that Sample Processing Control (SPC) failed. The sample was not properly processed, or Polymerase Chain Reaction (PCR) was inhibited.

ERROR: An ERROR indicates that Probe Check Control (PCC) failed, and the assay was aborted possibly due to the reaction chamber being filled improperly, a reagent probe integrity, syringe pressure issues, or failure of the CBNAAT module.

NO RESULT: A NO RESULT indicates that insufficient data were collected. For example, the operator stopped a test that was in progress.

RIF Indeterminate: RIF indeterminate result indicates that the sample has a less bacterial load.

Program guidelines recommend obtaining a second specimen to confirm rifampicin resistance in these scenarios

Xpert MTB/RIF assay for the diagnosis of pulmonary tuberculosis in children: a systematic review and meta-analysis. Detjen AK, DiNardo AR, Leyden J, et al. Lancet Respir Med. 2015;3:451–461. doi: 10.1016/S2213-2600(15)00095-8.